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WITH SALVARSAN, WITH SPECIAL REFERENCE
TO THE CLINICAL RESULT AND THE
WASSERMANN REACTION

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New York

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A STUDY OF FIFTY CASES OF SYPHILIS TREATED WITH SALVARSAN, WITH SPECIAL REFERENCE TO THE CLINICAL RESULT AND THE WASSERMANN REACTION

By ABR. L. WOLBARST, M. D.,

New York.

Through the courtesy of Geheimrat Professor Paul Ehrlich, the first injection of salvarsan was given by the writer, October 10, 1910. Since then the author has treated about 150 syphilitic patients with this remedy and carefully studied the results. A few patients have disappeared, some have taken mercury or iodides since salvarsan treatment, and some have been treated within a period of time too brief to be of much value in a paper of this kind. Such cases have therefore not been included in the present report. The cases herein reported have all been under observation, either by the writer or by the attending physician, for periods varying from four to ten months. This time is considered sufficient to warrant our drawing a fair conclusion as to the results obtained. The data herewith submitted were summarized up to August 15, 1911, nearly ten months since the first injection was given.

With but a few exceptions, all of these patients received but one injection of salvarsan. The intramuscular method of Alt (alkaline solution) was used in all except five cases, in which the intravenous method was employed. Careful attention was given to every detail, particularly, however, in reference to the clinical results and the effect on the Wassermann reaction. Wherever it was possible the blood was examined before the injection, and as often as practicable after. It will be observed that in quite a number of cases, though the patients were under observation clinically, the reaction was not determined because the patients refused to give their consent to the test.

In every case, without exception, a careful examination was made of the heart and kidneys, and in most cases the eyes were also carefully examined. Accurate reports were kept of the patients while in the hospital. The urine was examined every four hours, with special reference to the occurrence and elimination of arsenic and the presence of albumin. It may be said here that arsenic was found in nearly every case within from eight to fourteen hours, and that elimination ceased at the end of from eight to ten days. In a few cases a slight tendency to urinary suppression was noted, which quickly gave way to the administration of diuretics. In not a single instance did albumin make its appearance in the urine after the injection; in fact, in most of the cases, the preexisting albuminuria disappeared soon after the treatment. All patients were kept in bed at least four or five days, and many of them remained in the hospital about ten days. Treatment was not administered in any case that did not show a distinct, palpable lesion traceable to syphilis.

1. *By effects:* There were no alarming by effects

or secondary phenomena of any importance in this series of cases, except in one case (Case xxvii). This patient exhibited an unusually severe reaction to the remedy, characterized by the development of a high temperature (105.4° F.), an extensive scarlatinal eruption, and marked urinary suppression. All of these symptoms responded readily to the administration of diuretics. Chills, vomiting, diarrhoea, collapse, and similar phenomena that have been described by other writers were conspicuous by their absence. In not a single instance was a normal eye affected by the drug, and in only one case (xlii), the existing optic atrophy was apparently stimulated in its progress and total blindness ensued. It is not fair to ascribe this outcome to the salvarsan alone, in view of the rapidity of the atrophic process before the injection. In one case (xlv), peroneal paralysis and sciatic neuritis, with degeneration, followed the second injection. In not a single case did necrosis or abscess develop; the average reaction temperature did not exceed 101.5° F.; the Jarisch-Herxheimer appeared in about five per cent. of the cases. Pain was a frequent sequel to the injection, but in no case was it severe enough to cause alarm. In one case (xxiv), it persisted several months, in the form of a stiffness in the gluteal region, which made it difficult for the patient to tie the strings of his shoes. In most cases the pain disappeared within ten days to two weeks, and some of the patients exhibited no pain whatever after the second or third day.

2. *Doses.* With a view of determining what effect, if any, the dose has upon the clinical result these data are presented:

16 patients received 0.6 gramme.
29 patients received 0.5 gramme.
4 patients received 0.45 gramme.
1 child received 0.25 gramme.

Of the 27 patients in whom a clinical "cure" was observed,

10 patients received 0.6 gramme,
17 patients received 0.5 gramme,
an average dose of 0.54 gramme.

Of the 10 patients who improved, without clinical recurrence,

1 patient received 0.6 gramme,
6 patients received 0.5 gramme,
2 patients received 0.45 gramme,
1 patient (child) received 0.25 gramme,
an average (excluding the child's) of 0.5 gramme.

Of the 10 patients who improved, with clinical recurrence later,

3 patients received 0.6 gramme,
5 patients received 0.5 gramme,
2 patients received 0.45 gramme,
an average of 0.5 gramme.

Of the 3 patients who showed no benefit from the treatment,

- 2 patients received 0.6 gramme,
1 patient received 0.5 gramme,
an average dose of 0.56 gramme.

It is thus to be noted that there was no appreciable difference in clinical result between the patients who received the standard dose, 0.6 gramme, and those who received less. The result was about the same in all cases, irrespective of the slight difference in dose.

3. The period of observation:

Cases under observation	10 months,	1 case
Cases under observation	9 months,	6 cases
Cases under observation	8 months,	8 cases
Cases under observation	7 months,	8 cases
Cases under observation	6 months,	9 cases
Cases under observation	5 months,	10 cases
Cases under observation	4 months,	7 cases
Cases under observation	3 months,	1 case

An average period of observation of 6.4 months.

In addition to these fifty cases, we may consider three cases which presented somewhat unusual features, but which were not observed for any length of time. These will be mentioned in detail at the end of this paper.

4. The stage of the disease: These cases have been divided for classification purposes into five stages or classes, viz.: primary, secondary, tertiary, inherited, and parasyphilitic. Thus:

Primary syphilis,	6 cases
Secondary syphilis,	14 cases
Tertiary syphilis,	14 cases
Parasyphilis,	14 cases
Inherited syphilis,	2 cases

Total,50 cases

The primary cases were under observation as follows:

9 months,	2 cases
8 months,	1 case
7 months,	1 case
6 months,	1 case
5 months,	1 case

An average of 7.4 months.

The secondary cases were under observation as follows:

10 months,	1 case
9 months,	1 case
8 months,	3 cases
7 months,	2 cases
6 months,	1 case
5 months,	4 cases
4 months,	2 cases

An average of 7 months.

The tertiary cases were under observation as follows:

9 months,	1 case
8 months,	1 case
7 months,	3 cases
6 months,	2 cases
5 months,	2 cases
4 months,	4 cases
3 months,	1 case

An average of 7.6 months.

The parasyphilitic cases were under observation as follows:

9 months,	2 cases
8 months,	2 cases
7 months,	2 cases
6 months,	4 cases
5 months,	3 cases
4 months,	1 case

An average of 6.5 months.

The inherited cases were under observation as follows:

8 months,	1 case
6 months,	1 case

An average of 7 months.

The parasyphilitic cases were all cases involving the brain and spinal cord, without the presence of distinctly typical syphilitic lesions. The hereditary cases were both in children, in whom there was a distinct history of syphilis in one or both parents, and in one instance the syphilitic ancestry could be traced back three generations.

5. The clinical results obtained:

Patients who have been apparently "cured" clinically, 27 (54 per cent.).

Patients who have improved materially, without recurrence, 10 (20 per cent.).

Patients who have improved, but clinical recurrence developed, 10 (20 per cent.).

Patients who have not been influenced by the treatment, 3 (6 per cent.).

From these data it will be seen that seventy-four per cent. of the patients treated were either "cured" clinically or greatly improved, without a recurrence lasting over a period averaging about seven months. By clinical "cure," we mean that condition in which the clinical manifestations of the disease have disappeared and the patients feel perfectly well. This clinical "cure" does not take into account the Wassermann reaction, inasmuch as I believe that it is possible to be "cured" of syphilis, in the clinical sense, and still present a positive seroreaction. It is also recognized in this classification that an absolute "cure" for syphilis is still something to be wished for; nevertheless, it is safe to consider such patients "cured" clinically, for present purposes, when they have gone for long periods without showing any recurrence of their former or new lesions. That these patients have been under observation a sufficient length of time to justify our conclusion may be seen from these data:

Of the 27 cases considered "cured" clinically, 1 case has been under observation 10 months, 3 cases have been under observation 9 months, 6 cases have been under observation 8 months, 5 cases have been under observation 7 months, 4 cases have been under observation 6 months, 5 cases have been under observation 5 months, 3 cases have been under observation 4 months. An average of 7 months.

Of the 10 cases "improved" without recurrence, 2 cases have been under observation 8 months, 2 cases have been under observation 7 months, 1 case has been under observation 6 months, 1 case has been under observation 5 months, 3 cases have been under observation 4 months, 1 case has been under observation 3 months. An average of 5.6 months.

Of the 10 cases "improved" and followed by recurrence, 3 cases have been under observation 9 months, 2 cases have been under observation 6 months, 4 cases have been under observation 5 months, 1 case has been under observation 4 months. An average of 6.3 months.

6. The stage of the disease and the clinical result:

Result.	Pri- mary.	Sec- ondary.	Ter- tiary.	Para- syphi- litic.	Heredi- tary.	Total.
"Cured"	5	11	6	5		27
Improved			6	3	1	10
Improved with recurrence. I		3	2	4		10
No change				2	1	3
Totals	6	14	14	14	2	50

This table indicates that of six primary cases five patients were "cured" and one suffered a recurrence (Case xxxviii) eight months after the injection; of

the fourteen secondary cases eleven patients may be considered "cured" and three suffered recurrence; among the tertiary cases twelve patients were either "cured" or improved, without recurrence, and but two suffered recurrence; and among the fourteen parasyphilitic cases eight patients were either "cured" or improved without recurrence, four suffered recurrence, and in two no change was noted. I believe this to be a remarkable evidence of the potency of the remedy, in view of the comparatively small doses (but one injection) and the long period under which these cases have been observed.

7. Period of time after injection when recurrence took place:

In 1 case recurrence occurred 8 months after injection.
In 1 case recurrence occurred 7 months after injection.
In 1 case recurrence occurred 4 months after injection.
In 3 cases recurrence occurred 3 months after injection.
In 1 case recurrence occurred 2 months after injection.
In 3 cases recurrence occurred 1 month after injection.
An average period of 3.3 months.

Here again we note that one injection has been capable of preventing the development of syphilitic lesions for periods varying from three to ten months. The recurrent cases will be mentioned in detail later. It is a fair inference that all or the greater part of these recurrences might have been prevented if a second injection had been given a month after the first, thereby obtaining a *sterilisatio magna* instead of a *sterilisatio fractionata*.

8. As to the Wassermann reaction:

In 36 cases the reaction was positive before treatment: Of these, 12 remained positive, or became so after becoming negative (33 per cent.); 11 became negative and remained so, for the entire period of observation (30 per cent.); 12 were not examined for the reaction; 1 became negative after the second injection.

In 2 cases the reaction was negative before treatment: Of these, 1 remained negative after the injection, and 1 became positive after the injection.

In 12 cases the reaction was not determined before the injection: Of these, 6 were negative after the injection, 2 were positive, 4 were not examined for the reaction.

In other words, in thirty-six positive cases the positive reaction remained unaffected in thirty-three per cent., and changed to negative in thirty per cent. These reactions were observed for various periods, as follows:

1 case remained negative 9 months after the injection.
1 case remained negative 8 months after the injection.
1 case remained negative 6 months after the injection.
3 cases remained negative 5 months after the injection.
2 cases remained negative 4 months after the injection.
3 cases remained negative 1 month after the injection.
An average of 4.5 months.

Of the 12 cases that remained positive after the treatment, 2 cases remained positive 8 months after the injection, 1 case remained positive 7 months after the injection, 2 cases remained positive 5 months after the injection, 2 cases remained positive 4 months after the injection, 1 case remained positive 3 months after the injection, 3 cases remained positive 2 months after the injection, 1 case remained positive 1 month after the injection. An average of 4.3 months.

It is thus seen that in twenty-three cases with a positive reaction, eleven cases became negative and remained so for periods averaging 4.5 months, while twelve cases either remained positive or became so after having become negative after periods averaging 4.3 months. This again, I believe, to be a very commendable evidence of the potency of one

intramuscular injection of salvarsan. Surely no other preparation of arsenic or of mercury can equal these results after one treatment.

9. The relation between the clinical results and the reaction:

In the 27 cases considered "clinically cured," the reaction became negative in 11 cases (41 per cent.); the reaction remained positive in 8 cases (30 per cent.);¹ the reaction was not observed in the remainder.

In the 10 cases in which improvement was noted, without clinical recurrence, the reaction became negative in 4 cases (40 per cent.); the reaction remained positive in 2 cases (20 per cent.); the reaction was not observed in the remainder.

In the 10 cases in which improvement was followed by a clinical recurrence, the reaction became negative in 3 cases (30 per cent.); the reaction remained positive in 5 cases (50 per cent.); the reaction was not observed in the remainder.

In the 3 cases in which no clinical change was noted, the reaction remained unchanged.

These figures indicate that in thirty-seven cases in which a "clinical cure" or a decided improvement without clinical recurrence was seen, the reaction changed from positive to negative in fifteen cases (forty-one per cent.), and remained positive or became so after having changed to negative in ten cases (twenty-seven per cent.); whereas in those cases in which improvement was followed by a clinical recurrence, the reaction changed to negative in but thirty per cent. of the cases and remained positive in fifty per cent., thus showing that there is a definite relationship between the clinical improvement and the change in reaction. We may assume from these data that salvarsan has the effect of changing the seroreaction from positive to negative in direct proportion to the clinical improvement, or, in other words, that the change in reaction goes hand in hand with the change in the clinical condition.

10. The relation between the reaction and the stage of the disease:

In the 6 primary cases, the reaction became negative in 2 cases (33 per cent.); the reaction remained positive in 3 cases (50 per cent.); the reaction was not observed in the remainder.

In the 14 secondary cases, the reaction became negative in 7 cases (50 per cent.); the reaction remained positive in 5 cases (36 per cent.);² the reaction was not observed in the remainder.

In the 14 tertiary cases, the reaction became negative in 2 cases (15 per cent.); the reaction remained positive in 3 cases (22 per cent.); the reaction was not observed in the remainder.

In the 14 parasyphilitic cases, the reaction became negative in 7 cases (50 per cent.); the reaction remained positive in 5 cases (40 per cent.); the reaction was not observed in the remainder.

In the 2 hereditary cases, the reaction was not observed after the injection.

If these data signify anything, they make it appear that there is no definite relation between the stage of the disease and the seroreaction as far as the treatment with salvarsan is concerned. The best results, however, seem to have been obtained in the secondary and parasyphilitic stages, in which fifty per cent. of the cases changed from positive to negative.

¹One case became negative only after a second injection was given.

²One case became negative only after a second injection was given.

II. Table showing the seroreaction before and after treatment:

(a) Cases considered clinically cured.

Case No.	Reaction		Period after injection.
	before.	after.	
1	+	—	5 months
3	+	—	1 "
5	+	—	8 "
9	+	—	9 "
10	+	—	4 "
11	+	—	5 "
12	+	—	6 "
13	+	+	5 "
16	+	+	3 "
17	+	+	8 "
18	+	+	5 "
19	+	+	4 "
27	—	+	9 "
2	o	—	7 "
6	o	—	6 "
7	o	—	3 "
8	o	—	3 "
14	o	+	4 "
15	o	+	4 "

(b) Cases improved without recurrence.

28	+	—	1 "
29	+	—	5 "
30	+	—	1 "
33	+	+	1 "
36	+	+	2 "
31	o	—	3 "

(c) Cases improved, with recurrence.

41	+	—	4 "
38	+	+	8 "
39	+	+	7 "
40	+	+	2 "
42	+	+	2 "
43	+	+	4 "
46	—	—	6 "
45	o	—	1 "

NOTE: +, positive; —, negative; o, reaction not observed.

12. The character of the recurrences:

Recurrence took place in 1 primary case.

Recurrence took place in 3 secondary cases.

Recurrence took place in 2 tertiary cases.

Recurrence took place in 4 parasyphilitic cases.

The character of the recurrence varied in the individual cases.

1. CASE XXXVIII. *Primary*. Eight months after the injection, a few small mucous patches appeared on the lips. This was associated with a positive seroreaction.

2. CASE XXXIX. *Secondary*. Seven months after the injection, two minute ulcerations appeared on the tonsils, associated with a slight papular eruption on the forearm. Seroreaction, slightly positive.

3. CASE XLI. *Secondary*. Four months after the injection, the voice became hoarse and husky. There were no visible lesions of any kind. Noguchi reaction, negative.

4. CASE XLV. *Secondary*. One month after the injection, patient began to see dark spots before the eyes, which was diagnosed as syphilitic neuritis. Wassermann and Noguchi reactions, both negative.

5. CASE XL. *Tertiary*. Two months after the injection, the patient noticed a return of the redness of the nose and thickening of the skin, to a slight degree. Wassermann reaction, slightly positive.

6. CASE XLVII. *Tertiary*. One month after the injection, the obnoxious ozæna accompanying the destruction of the nasal tissues returned, after having disappeared.

7. CASE XLII. *Tabs*. Three months after injection, the pains and ataxia returned with renewed vigor, and optic atrophy became markedly worse.

8. CASE XLIII. *Paresis*. Three months after injection, the improvement, which was very marked, suddenly gave way to a return of all his parietic symptoms. This change was coincident with a slight cerebral hæmorrhage.

9. CASE XLIV. *Syphilitic Gastritis*. The symptoms returned three months after the injection. Wassermann and Noguchi reactions were both positive.

10. CASE XLVI. *Tabs*. For a month the pains and vomiting had ceased, but at that time a gastric crisis set in, accompanied by all the previous symptoms.

13. Therapeutic effect of salvarsan:

There can be no denying the wonderful effect of salvarsan on syphilitic conditions. Undoubtedly experience is teaching us that a single injection of salvarsan has the potency of a thorough course of mercury and iodides. That one injection will cure syphilis, it would be folly to expect in the light of our experience, but I feel safe in saying that we may hope to cure syphilis, clinically and serologically, after we have learned all that this marvellous remedy is capable of doing. We are still uncertain in regard to the best method of administration, the proper dose, the number of times it should be given, and the interval of time between injections. Time alone can determine these important facts for us. Time will also tell us whether it is best to give salvarsan alone or combined with mercury, for we have not yet reached that point where we may with safety relegate this old time specific to the rear. Apparently the best results are to be obtained by a judicious use of both remedies combined, but the exact method of procedure must be left to future experience to decide.

In the meantime, we are justified in adopting certain routine methods in cases in which the treatment is deemed suitable. The intravenous injection is by far the most agreeable from the patient's standpoint, and is probably the most effective mode of administration. It should be carefully given and repeated once or twice at intervals of two or three weeks. For the sake of further security, though I have not found it necessary, it is well to precede and follow these injections with a course of mercurial inunctions or injections. Next to the intravenous method, the intramuscular injection of an iodipin emulsion is the most desirable, but it is still to be proved that it is as effective as the intravenous or the alkaline intramuscular method. It has the single advantage, if that is one, that the treatment may be given by the physician in his office, and the patient may then go home. I am not at all certain that it is wise or even safe to do this.

A brief clinical review of the fifty cases constituting this study will be of interest:

(a) Cases in Which a Clinical "Cure" Followed the Injection of Salvarsan:

CASE I. *Primary Syphilis*: S. H., male, aged twenty-three years. Referred by Dr. L. T. Ashcraft, of Philadelphia. Infected one month. Wassermann reaction, +. November 29, 1910, received 0.6 gramme. No pain whatever, but it became very severe the next day. Maximum temperature 102.4° F., on the second day. Left the hospital in twelve days. Wassermann reaction, December 28th, —; March 22d, —; May 3d, —, patient clinically well. On August 3d, Dr. Ashcraft stated that the man had not presented any clinical symptoms since the last report. Period of observation, eight months.

CASE II. *Secondary Syphilis*: G. A., male, aged twenty-four years. Macular eruption on body, duration ten days; chancre still visible, though disappearing; duration six weeks. No Wassermann reaction taken. Injected, January 4, 1911, at People's Hospital, 0.6 gramme. Slight pain, which soon disappeared. January 24th, site of chancre marked by a pinkish discoloration of the skin; eruption gone. Patient reappeared for examination, May 19, 1911. Felt well in every respect. Wassermann reaction, —. August 8, 1911, patient perfectly well. Wassermann and Noguchi reactions, both negative. Period of observation, seven months.

CASE III. *Primary Syphilis*: I. L., male, aged twenty-

five years. Referred by Dr. T. Parodi. Chancre on upper lip. Duration, six weeks; no secondary lesions. Wassermann reaction, two tests, +; Noguchi reaction, two tests, +. Injected, February 14, 1911, at St. Mark's Hospital, 0.6 gramme; moderate pain. Within ten days the lesion had entirely disappeared, and the mucous membrane of the lip seemed normal. March 27, 1911, Wassermann and Noguchi reactions, —. May 12th, patient stated that he felt perfectly well. There have been no secondaries. July 21, 1911, he reported by telephone that he felt perfectly well. On August 8, 1911, he reported the same. Period of observation, six months.



FIG. 1.—Illustrating Case IV. chancre of urinary meatus, before treatment.



FIG. 2.—Illustrating Case IV. Photograph taken forty-two days after injection of 0.6 gramme of salvarsan. Meatus absolutely normal. (See Fig. 1.)

CASE IV. *Primary and Secondary Syphilis*: S. H., male, aged twenty-three years. Chancre of urinary meatus. Typical hard, infiltrated. Duration, three and one half months; has had no constitutional treatment. Chancre surrounds entire meatus and extends backward into the urethra for half an inch (Fig. 1). Roseola present, but faded. Wassermann and Noguchi reactions, +. Injected, March 15, 1911, at St. Mark's Hospital, 0.6 gramme, intravenously (one of the few cases in this series in which the intravenous method was employed). May 10, 1911, reaction, negative; June 1st, patient reported for examination. The meatus was perfectly normal; patient had gained eighteen pound. Photograph taken forty-two days after injection shows a normal meatus (Fig. 2). July 20, 1911, patient reported feeling absolutely well. Period of observation, four months.

CASE V. *Secondary Syphilis*: G. F., male, aged twenty-seven years; mucous patches involving the mouth and pharynx; duration four months. Unaffected by injections of salicylate of mercury and inunctions. Wassermann-Noguchi reaction, +. November 22, 1910, at People's Hospital, 0.5 gramme. Slight pain. Patient left the hospital ten days later, in excellent condition. Returned for observation, May 12, 1911. Condition normal, without any recurrence of the patches. Had gained four pounds in weight, and felt perfectly well. Wassermann-Noguchi, negative. August 2, 1911, condition the same. Wassermann-Noguchi reaction, —. Period of observation, eight months.

CASE VI. *Secondary Syphilis*: L. B., male, aged thirty-eight years. Referred by Dr. B. Livingston. When first seen, the patient had a large, deep ulcer on the right lower lip, mucous patches in the mouth and pharynx, and a papular syphilide on the left side of the face and neck (Fig. 3). These lesions had appeared eight months previously, with the disappearance of the primary chancre on the penis. The patient had been treated with mercury in all of its forms, and was salivated several times in the hope of obtaining a recession of the lesions, but without avail. Apparently, this was a case with a decided constitutional antipathy to mercury, for the more treatment he received, the worse his condition became.

On November 19, 1910, at St. Mark's Hospital, the patient was injected with 0.5 gramme, hyperideal. Moderate pain, traces of which remained for several months. He

left the hospital ten days later, almost entirely recovered. The ulcer had disappeared altogether (Fig. 4) and the eruption on the face had become much less prominent and faded in color. Likewise the mucous patches in the throat had disappeared.

Since then there has been no recurrence whatever, and the patient considers himself perfectly well. The Wassermann reaction was not taken before the injection, owing to his being salivated at the time, but since the injection it has been taken four times as follows: December 20, 1910, negative; February 1, 1911, negative; March 7, 1911, negative; May 10, 1911, negative. The patient has gained twenty-five pounds in weight. When last seen, August 1, 1911, his face showed no traces whatever of the former syphilide. Period of observation, eight months.

CASE VII. *Secondary Syphilis*: L. S., male, aged thirty years. Referred by Dr. I. C. Rubin, with this history: For three months, patient has had mucous patches covering entire palate, uvula and pharynx; a pustular syphilide covering the face and body. These lesions had faded away to some extent, under mixed treatment and inunctions, but the macular syphilide and adenitis still persisted. He did not stand mercury injections well.

February 14, 1911, at People's Hospital, he received 0.6 gramme. No pain at first, but severe pain later lasting several weeks. At the end of a week's stay in the hospital, he left, feeling much better—practically well, in fact. He has been under observation since then, and has had no recurrence. Wassermann-Noguchi reactions, May 18, 1911, negative. July 31, 1911, patient clinically well. Period of observation, five months.

CASE VIII. *Secondary Syphilis*: G. S., male, aged thirty-two years. Mucous patches in mouth, duration four months. Has been treated with inunctions, without benefit. March 7, 1911, at St. Mark's Hospital, received 0.5 gramme salvarsan. April 9, 1911, felt perfectly well, no recurrence; Wassermann-Noguchi reaction, —; May 28, 1911, also —. Had gained seven pounds in weight. July 10th, clinically well. Period of observation, four months.

CASE IX. *Cerebral Syphilis* (reported in the *Interstate Medical Journal*, January, 1911): A. A., male, aged twenty-nine years. Referred by Dr. Charles A. Spivacke, with this history: Family history negative as to syphilis.

Primary infection in 1905. Was treated for about six months with mercurial injections. No history of sore throat, alopecia, or pains in head. A year later the right elbow became painful and swelled a great deal. The pain was dull in character and so severe at night as to keep him awake. This condition improved under treatment.



FIG. 3.—Illustrating Case VI. Large deep luetic ulcer on lower lip, before treatment.



FIG. 4.—Illustrating Case VI. ten days after the injection of 0.5 gramme of salvarsan; no trace of ulcer visible. (See Fig. 3.)

Eighteen months ago patient suffered an attack of right hemiplegia while under the influence of alcohol. The right arm, leg, and right side of face were affected. In bed several weeks. Also suffered slight illusions at the time. He improved under a course of iodides, but felt very depressed and lost all ambition for work or play. The right elbow remained swollen and tender. Had been under treatment for some time at the Vanderbilt clinic.

I saw him first October 26, 1910. He was dull and apathetic, unable to do his work (bartender), losing one position after another. His face had a constant smiling, childish appearance. Had no illusions, but realized that

he was not well and wanted to do something that might enable him to go back to work to support his mother.

Physical examination as to viscera, heart and arteries, and urine, normal. The right elbow joint measured eleven inches in circumference, the left ten and a quarter inches. Eyes normal, except for a slight cloudy deposit on the anterior surface of lens of left eye, in upper right quadrant. Wassermann reaction ++.

November 3, 1910, at People's Hospital, received 0.5 gramme. Slight pain, which passed off next day. Temperature reaction quite active, never higher than 102° F., on the third day. Pulse varied from 70 to 94. Was out of bed most of the time. Improved markedly after the fourth day. His mind brightened up perceptibly, he took a greater interest in things about him, and expressed a strong desire to go home and back to work. He felt strong and able to do anything. No infiltration or tenderness at the site of injection.

November 8th, at my request, he wrote me a letter describing his condition. It was full of hope and optimism; in fact, it gave every evidence of being written by a man who had awakened out of a stupor and saw the light of day.

November 15th. Sent home. Much improved. His arm did not pain any more and there was but a slight difference in the measurement of the elbows. His mind was active and bright, and his mother felt that he was brighter than he had ever been.

Arsenic was found in the urine eight days after the injection, albumin negative throughout.

December 1st. Condition highly satisfactory in all respects. Wassermann reaction +++. Eyes normal.

December 31st, +++; April 17, 1911, negative; May 15th, negative. He felt perfectly well, though he tired easily.

August 1, 1911, felt well. Wassermann-Noguchi reactions, —. Period of observation, nine months.

CASE X. Repeated Abortions of Suspected Syphilitic Origin. Mrs. M. B., aged thirty years. Referred by Dr. S. W. Bandler. Patient had been married twelve years, and was the mother of one child, seven years old. Since the birth of this child she had had three miscarriages—two at six months and one at three months. Gynecological examination, negative. Wassermann reaction, strongly positive.

December 31, 1910, at Beth Israel Hospital, she received 0.5 gramme hyperideal. Moderate pain, which soon became very severe. Marked Herxheimer reaction. Patient reappeared for examination May 4, 1911, feeling perfectly well; Wassermann-Noguchi reactions, —. Noticed that her sexual feeling had changed considerably. Before the treatment, she was frigid and lacked sexual desire; since the injection, she had acquired a strong sexual feeling. Period of observation, four months.

CASE XI. Syphilitic Periostitis: J. W. E., male, aged thirty-seven years. Complained of severe racking pains in the forearms and legs, sufficient to keep him awake at night. Had lost much flesh, and weighed 117 pounds. Previous history somewhat indefinite as to primary lesion. He first noticed a sore throat which persisted in spite of local treatment. Under internal treatment, however, it disappeared. Since then was well until about a year ago, when the pains in the arms and legs came on. Since then he has lost twenty-five pounds. December 1, 1910, Wassermann reaction, +++; January 5, 1911, +++.

January 15, 1911, at St. Mark's Hospital, received 0.5 gramme salvarsan. Moderate pain, which persisted for a week. The pains in the bones soon left him, and up to the present writing (August 15th) they did not since return. Wassermann reaction, March 17th, negative; June 2d, negative. July 25th, clinically well. Period of observation, six months.

CASE XII. Disseminated Cerebrospinal Syphilis, with Symptoms Suggestive of Tabes, and with Hysteroid Symptoms: Mrs. L. E., aged thirty-six years. Referred by Dr. C. F. J. Laase, with the following history:

The patient was treated, fifteen years ago, for syphilis involving the throat. Primary lesion discovered on the genitals. Four years ago, she returned with the complaint of having severe rheumatic pains, which appeared all over the body at different times. These pains were associated with severe spasms or contractions of the muscles of her legs, arms, and neck. During these spells she

could not stand or walk, and when they affected the neck, her head was held stiff, sometimes turned to one side; easily becomes "hysterical" when excited. Now (December, 1910) her complaint was exactly the same, but in addition she had headaches, and she got spasms of the temporal muscles so that she could not close her mouth voluntarily, but must use her hand to do so.

All of these years, she had been going from one physician to another without relief, but she always failed to mention the specific infection fifteen years ago, until she returned to Dr. Laase for relief.

Dr. Laase gave her ten injections of salicylate of mercury, but she did not tolerate them well, though her symptoms were somewhat relieved by them. When the injections were suspended, the pains and spasms returned with renewed frequency and severity. Her eyes have been examined many times, and always found normal. Wassermann reaction (German Hospital) ++++.

November 26, 1910, examination by Dr. B. Onuf, suggested the diagnosis mentioned above. Salvarsan was advised, rather as an experiment than with any expectation of success.

December 7, 1910, at St. Mark's Hospital, I injected 0.5 gramme. Slight pain at first, which gradually increased, and remained fairly moderate for several days.

January 7, 1911, Dr. Laase reported: "She feels better than she has for some time, although she still experiences some of her former pains; but they are not severe enough to keep her in bed."

January 27th, Dr. Laase stated that "she reports decided relief from her pains. While at times she experiences some pains, they are bearable, being nothing in comparison with her previous suffering. The Wassermann reaction, on January 16th, was negative."

March 29th, Dr. Laase gave the patient an intravenous injection and on May 8th, he stated: "I saw her yesterday, and it seems that according to her report and her husband's observation, she has improved to the extent of ninety per cent., in that she seldom gets the pains complained of and then only for the brief space of a few hours."

June 1st, Wassermann and Noguchi reaction, both —. July 30th, clinically well. Period of observation, eight months.

CASE XIII. Primary Syphilis: S. B., male, aged thirty years. Referred by Dr. Henry Schumer. Duration of initial lesion two weeks; no secondaries. General adenopathy. Initial infection consisted of two distinct typical indurated chancres situated at the pubic crest. Wassermann reaction, +. December 20, 1910, at People's Hospital, 0.5 gramme. Considerable pain, which passed off the next day. Within two weeks the lesions disappeared, and the patient had been perfectly well since. There had been no secondaries at any time. Patient had been traveling, and returned to town on May 29, 1911. No clinical recurrence of any kind. Wassermann-Noguchi reactions, ++++.

Because of this positive seroreaction, I gave him an intravenous injection of 0.6 gramme June 3d, at St. Mark's Hospital, and another July 22d. Period of observation, seven months.

CASE XIV. Secondary Syphilis: F. V. E., physician, aged twenty-five years. Macular and papular roseola, three weeks' duration. Primary lesion barely visible. January 6, 1911, at People's Hospital, injected 0.6 gramme, Alt method. No pain. The patient left the hospital about a week later feeling splendid. Roseola entirely gone. March 14, 1911, Wassermann-Noguchi reactions, —; patient has gained ten pounds; May 1st, clinically well. Wassermann-Noguchi reactions, —. As a result of this test, he was given an intravenous injection on May 15th. August 2, 1911, he wrote, saying that he never felt so well nor looked as well as at present. Period of observation, seven months.

CASE XV. Secondary Syphilis: M. B. R., male, aged twenty-six years. Papular roseola, duration two weeks. Primary lesion still visible. Few mucous patches on tonsils and in mouth. On January 10, 1911, at St. Mark's Hospital, was given 0.6 gramme. Slight pain, which soon passed off. The erosions in the mouth disappeared within twenty-four hours, and the eruption passed off within a week. He left the hospital and went West on business. He was referred for further observation to Dr. M. A.

Fechheimer, of Detroit, who reported on May 16th as follows: "Patient shows no external manifestations of the disease. The Wassermann test was positive." On July 27th, reported feeling perfectly well. Here we have

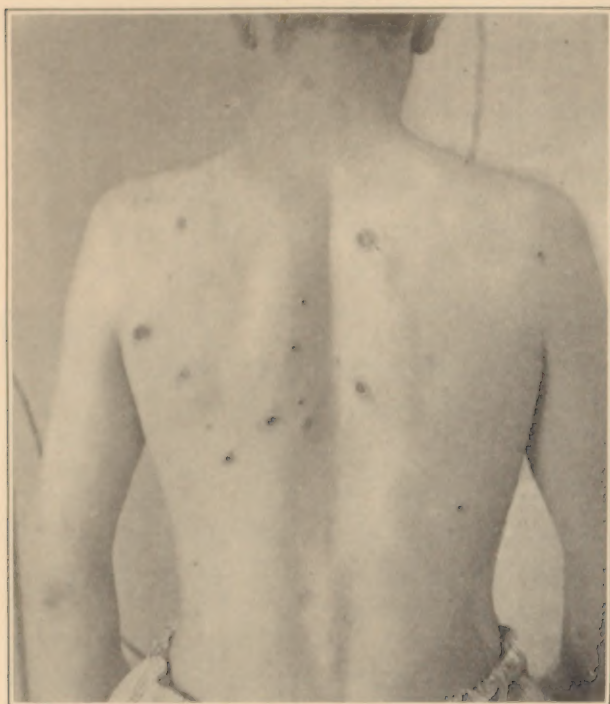


FIG. 5.—Illustrating Case XVII. Crust covered pustules on back, resisting treatment for four months.

another case of clinical "cure," with a positive reaction. Period of observation, six months.

CASE XVI. *Secondary Syphilis*: M. J. S., male, physician, aged twenty-eight years. Infected five months previously; three weeks after primary lesion appeared. Wassermann reaction was positive. Had been under bichloride injections, but did not stand them well. His physician advised salvarsan. On February 28, 1911, at St. Mark's Hospital, was given 0.6 gramme intravenously. Wrote from home, April 10th, that he was feeling better than ever, but a Noguchi test made a few days previously was positive. A second intravenous injection was therefore given by Dr. Holliday, of Pittsburgh, on April 23, 1911. June 5, 1911, Noguchi reaction, —. Clinically well. July 31, 1911, perfectly well. Period of observation, five months.



FIG. 6.—Illustrating Case XVII. Luetic ulceration of the great toe with loss of nail, in spite of vigorous treatment with mercury and iodides.

slowly changed to pustules, and were not influenced by treatment. Condition, October 1, 1910, pustules on back, ranging in size from a dime to a quarter; dried slowly, and became scaly (Fig. 5). Mucous patches on tongue since July remained and became ulcerous. Slough over both tonsils during August and September. Left iritis since September 15th. Ulceration on great toe (Fig. 6) since early in September. Nail removed October 14th. He had lost much flesh and strength.

Treatment: Mercury succinamide, grain $\frac{1}{2}$, three times weekly, by hypodermic injection; 15 injections; no result. Salivated first two weeks in August. Last two weeks in August, protoiodide of mercury, grain $\frac{1}{2}$ by mouth; salivated again. Inunctions since September 7th. 15 (30 grains), 8 (40 grains); also potassium iodide. No effect. October 16th, Wassermann reaction ++++.

October 17th, at the People's Hospital, received 0.5

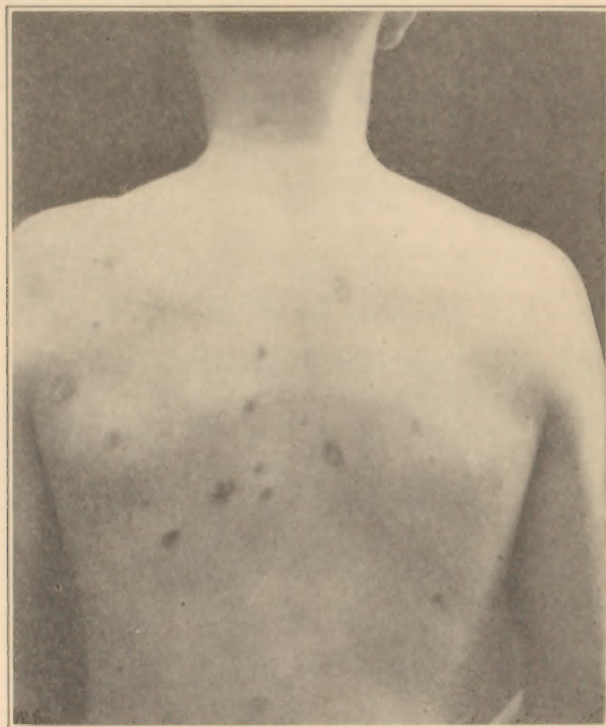


FIG. 7.—Case XVII. Photograph taken twelve days after the injection of 0.5 gramme of salvarsan. Crusts and scales have disappeared and left nothing but a pinkish coloration of skin. (See Fig. 5.)

gramme. Pain moderate, radiating principally down the thighs, and controlled by hot water bag on buttocks. Reaction not marked. Uneventful stay in hospital; up and about on the second day. Temperature highest on second day (99.8° F.). No infiltration nor redness at site of injection. Tender on pressure.

Examination of eyes, by Dr. M. Rosenbaum: "October 24th, syphilitic iritis of left eye; slight circumcorneal injection, posterior synechiae, cloudiness of vitreous. October 28th: Cloudiness of vitreous disappeared, iritis not present; posterior synechiae fading. Right eye normal; left eye, vision 12/70 with atropine. November 3d: Both eyes normal."

Discharged from hospital October 29th. Skin lesions but faintly visible; pink spots on back. Scaling all disappeared. Great toe granulating. (Fig. 7.)

November 18th: Eyes normal; skin still showed pink areas where the ulcers formerly were. Patient had gained nearly fourteen pounds. Big toe nearly well, with new nail rapidly coming out.

December 13th: Skin clear; toe practically well; eyes normal. Wassermann reaction ++.

June 26, 1911 (eight months after the injection)



FIG. 8.—Case XVII. Photograph of toe (see Fig. 6) taken eight months after the injection of 0.5 gramme of salvarsan. The ulcer has disappeared and a perfect nail has taken its place.

the patient was feeling perfectly well, eyes normal, and the great toe had grown to its normal size and condition (Fig. 8). Wassermann-Noguchi reaction, ++. August 8, 1911, he reported no change in his condition. Period of observation, ten months.

CASE XVIII. *Tertiary Syphilis Involving the Nasal Septum and the Hard Palate*: Mrs. S. B., aged thirty-seven years. Referred by Dr. L. S. Blumberg, of Newark, N. J., with this history: Patient denied ever having had syphilis knowingly; first noticed trouble in the mouth a year ago. Three months later, she passed a small bone from the nose through the hard palate, which left a perforation about an eighth of an inch in diameter. This had partially closed under antisyphilitic treatment. About eight months ago the nasal septum broke down, and the process had been going on since then. Eleven months ago her sixth baby was born, perfectly well, and remained so. For many years she suffered from pain in the gall-bladder region, but on operation a necrosed area was found, which was thought to be gummatous in character. The mass was undisturbed, and the wound closed up. Since then she has felt better. December 4, 1910, Wassermann reaction, ++++. December 12th, at People's Hospital, she received 0.5 gramme. Moderate pain, which soon passed off.

The patient then went to her home in Newark, and was not heard from until May 24, 1911, when Dr. Blumberg wrote as follows, concerning her: "She is now enjoying good health. Since the treatment she has gained thirty-five pounds in weight, is doing all her housework, besides helping her husband in his store. The perforation of the hard palate has decreased in size from that of a dime to the diameter of a small pencil, and there is no more foul discharge. The destruction of the nasal septum, while complete, has been arrested, and a plastic operation to correct the deformity will be done very shortly. May 21st a Wassermann-Noguchi test proved strongly positive." August 9th Dr. Blumberg wrote: "She is enjoying very good health at present. Is gaining in weight and looking splendid." Here, too, we have an excellent clinical result, with a strong positive reaction. Period of observation, eight months.

CASE XIX. *Syphilitic Periostitis*: H. W., male, aged thirty-two years. Complained of severe pains in the extremities, especially at night, associated with indefinite pains in the head at various times. Otherwise well, except that he is drowsy and could not apply himself to his work as well as he should. Had initial lesion nine years ago, and was treated on and off since then for about five years with mercury and iodides. Since stopping the treatment, his appetite had been poor, he was very nervous and complained of the pains mentioned before. Married five and a half years, wife never pregnant. November 17, 1910, Wassermann-Noguchi tests, +; December 19, 1910, ++++. January 5, 1911, at St. Mark's Hospital, received 0.6 gramme. No pain. Called for observation several times, and improved continually. May 9, 1911, stated that he felt excellent, his nervousness gone, pains absent, and appetite and sleep excellent. Had gained weight. Nevertheless, Wassermann and Noguchi tests, both ++. Refused further treatment. June 7, 1911, clinically well. Period of observation, five months.

CASE XX. *Precocious Tertiary Syphilis*: L. C., male, aged thirty-four years. Referred by Dr. M. J. Klein, with the following history: The patient was infected two years previously. Three months later a severe extensive vesiculopapular eruption developed, covering the entire body and face, associated with a gummatous infiltration of the epiglottis and the tonsils. The treatment at that time consisted of injections of cypridol, alternating with salicylate of mercury, with increasing doses of sodium iodide up to three drachms three times daily; also local applications to the throat. The general condition was not much improved by this treatment, although the lesions in the throat did show some betterment. The eruption on the face and extremities remained, however, and soon localized itself on the forehead, lobe of the ears, and on the legs and hands. Here there was actual loss of tissue, which was not influenced in the least by the treatment. At this time he was getting an injection of mercurv every second day, and was taking in addition the yellow iodide of mercury pills, grain $\frac{1}{6}$, from nine to

twelve daily. At no time did he show any symptoms of salivation. At various times he was given injections of enesol, bichloride and succinamide of mercury, and inunctions, all without effect. The ulcers on the hand and leg of the patient, just before receiving the injection of salvarsan, are well shown in the accompanying photographs (Fig. 9).

Wassermann-Noguchi reactions, ++. October 12, 1910, at the People's Hospital, he was given 0.5 gramme. Had slight pain, which soon disappeared. At the end of ten days he left the hospital, much improved. Fig. 10, taken five days after the injection, indicates the rapidity of the action in this case. The ulcers, which had previously been from $\frac{1}{4}$ to $\frac{1}{2}$ inch in depth, were now even with the surface and complete epidermization followed in a few days. This patient did not reappear for observation, but Dr. Klein who saw the patient several times, reported, August 2, 1911, more than



FIG. 9.—Illustrating Case XX. Luetic ulcers of hand and leg, resisting vigorous treatment. The ulcers were half an inch in depth.



FIG. 10.—Case XX. Photograph taken five days after injection of 0.5 gramme of salvarsan. Ulcerating cavities have been filled with granulating tissue which is even with the surface of the skin.

nine months after the injection, that he was perfectly cured, clinically, and had grown very stout. Period of observation, nine months.

CASE XXI. *Tertiary Syphilis with Extensive Syphilide*: Mrs. D. B., aged forty-five years. Married twenty-seven years, and had three children, all well. Had three miscarriages, years ago. First noticed bad sore throat six years ago. Was never sick before that time. The angina was followed by a skin eruption (red rash), which lasted a week, and disappeared under internal treatment. Patient took this medicine two years. For one year, was apparently well, but at that time ulcers began to break out, first in the face, and then on the left hand and arm. The face ulcers healed, but those on the hand and arm have remained ever since (three years). Had lost forty pounds in weight, but regained it. Had not taken medicine in three months, and felt greatly discouraged. The throat had been well since the first attack; there had been no alopecia, or headaches.

When first seen by me she presented enormous crust covered syphilides involving the left shoulder and arm.

and forearm and hand (Fig. 11). Wassermann and Noguchi reactions, both ++++. Urine contained faint traces of albumin, no sugar.

January 25, 1911, at St. Mark's Hospital, she received 0.5 gramme. Slight pain, which soon disappeared. Within a few days the syphilide began to show evidences of improvement, and on February 11th, seventeen days after the injection, the scales had disappeared, and healing was



FIG. 11.—Illustrating Case XXI. This photograph shows but one of many large crust covered syphilides, covering shoulder and arm, before treatment.

well under way (Fig. 12). This woman refused to present herself for further observation, in spite of every effort to have her do so, but on June 23, 1911, her husband stated that she was absolutely well. Period of observation, five months.

CASE XXII. *Syphilitic Osteomyelitis*: G. W., male, aged forty years. In the service of Dr. L. J. Ladinski, at Gouverneur Hospital. For twenty years, this man had suffered from an osteomyelitis of the forearm, which had resisted operative treatment of all kinds. When I saw him, on the invitation of Dr. Ladinski, he had two or three sinuses extending into the bones of the forearm, which had been operated on without benefit. The Wassermann reaction being strongly positive, it was decided to give him an injection of salvarsan.

December 10th, at Gouverneur Hospital, I injected 0.5 gramme hyperideal. He had moderate pain, which soon passed off. Temperature reaction, moderate. Within nine days he gained five pounds in weight, and the wounds showed signs of closing up.

This patient left the hospital well, and did not reappear for observation until May 29, 1911. On that day, five months after the injection, the sinuses in the arm were closed entirely and the man considered himself entirely well. He had gained much weight and felt fine. He refused to have a Wassermann test made. July 21, 1911, he reported, perfectly well. Period of observation, seven months.

CASE XXIII. *Syphilitic Alopecia*: H. E. E., male, aged

twenty-two years. Referred by Dr. S. J. Bernfeld. History: Primary infection uncertain, but apparently about four months ago. Secondaries never present. First noticed loss of hair about three months ago; has been under mixed treatment with slight benefit. Wassermann reaction (Dr. George F. Dixon), positive.

December 12, 1910, at the People's Hospital, he received 0.6 gramme hyperideal. No pain at any time. Sat up out of bed next day. Photograph taken immediately before the injection showed the typical alopecia. The patient left the hospital and soon disappeared. On July 25, 1911, Dr. Bernfeld heard from him from Europe, to the effect that he was feeling well and that his hair had returned to its normal condition. Period of observation, seven months.

CASE XXIV. *Tertiary Syphilis Involving the Tongue*: K. J., male, aged fifty-five years. For twelve years he had been suffering from leucoplakia of the tongue and syphilides in the mouth and on the face and neck. Primary infection obscure. Had been taking iodides and mixed treatment, with temporary benefit. Had lost much weight and now weighs but 122 pounds. Had numerous small mucous patches in the mouth and throat, and a copper colored syphilide scattered over the face and neck. The tongue was grooved and covered with white patches.



FIG. 12.—Illustrating Case XXI. Photograph taken seventeen days after the injection of 0.5 gramme of salvarsan. The crusts have entirely disappeared, leaving a smooth surface. These syphilides have since disappeared altogether.

Wassermann reaction, weakly positive (he had been taking iodide up to a few weeks ago).

November 27, 1910, at the People's Hospital, he received 0.5 gramme. Moderate pain, which increased and lasted for several months, making it impossible for him to bend or stoop. This pain eventually passed off.

He left the hospital, much improved.

January 19, 1911 (two months after the injection) he wrote: "I feel perfectly well, so much so that I commence to think of the future. I have still some pain in

my loins (caused by the injection), but am now able to put on my shoes without assistance, but of the dread disease there is no trace left. Altogether I am of the



FIG. 13.—Illustrating Case XXVI. Uvula, tonsils, and palate covered with a greenish white, membranous ulceration, which had resisted treatment for nearly two years. Within seventeen days after the injection of 0.5 gramme of salvarsan the mouth and throat were absolutely normal.

impression that I am perfectly cured." Did not reappear for another blood test.

May 26, 1911, he reported feeling well in every way. Period of observation, six months.

CASE XXV. *Secondary Syphilis*: P. A., male, aged twenty-eight years. Referred by Dr. M. J. Klein. Macu-

lopapular eruption all over the body, duration two weeks. Primary lesion still visible.

November 7, 1910, at the People's Hospital, received 0.5 gramme. No pain. Patient left the hospital in six days, feeling well. The eruption had nearly entirely disappeared.

March 12, 1911 (four months after the injection), he reappeared for observation, feeling well except for occasional pains in the forearm. Refused to have blood test made. There had been no secondary phenomena. Period of observation, four months.

CASE XXVI. *Malignant Secondary Syphilis Resisting Mercury and Iodides* (reported in the *Interstate Medical Journal*, January, 1911): J. L., male, aged twenty-eight years. Referred by Dr. J. B. Prager. Initial infection eighteen months ago, on the penis. Began as a pustule, which grew large and hard and eventually broke down, resisting treatment for seven months. Inguinal glands swollen and tender. Six weeks later, the roseola appeared and disappeared only after several months of treatment. For the past three months the patient complained of a sore throat, growing worse all the time, so that it interfered with his speech and rendered swallowing difficult and painful. Had also had pains in the joints.

Examination of the eyes, heart, lungs, and kidneys negative. Wassermann reaction +++.

Examination of the throat revealed a large greenish white, ulcerating area covering the uvula, tonsils, post-pharyngeal space, and part of roof of the mouth (Fig. 13). The mouth could be opened only with difficulty.

November 3, 1910. Injected 0.5 gramme hyperideol. No pain at time of injection, but a few hours later pain of moderate severity over the site of injection which lasted two days. Throat was cleansed with saline solution.

November 5th, improvement noted. Green ulceration turning paler and assuming a brownish color. Throat felt better, swallowing and speech easier.

November 10th, improvement continuous. Full diet. Out of bed and felt better in every way. Ulcerated area assuming normal color. No infiltration nor redness at site of injection.

November 15th, left the hospital feeling perfectly well, though the throat still showed some signs of the recent ulceration.

November 20th, throat normal.

November 25th, throat normal, and patient back to work. Gained seven pounds. Did not return for further observation.

April 15, 1911 (five months after the injection). Dr. Prager saw the patient, and stated that he was feeling perfectly well and that he had gained at least thirty pounds in weight. This information was corroborated by my own observation on July 23d. He felt perfectly well; blood

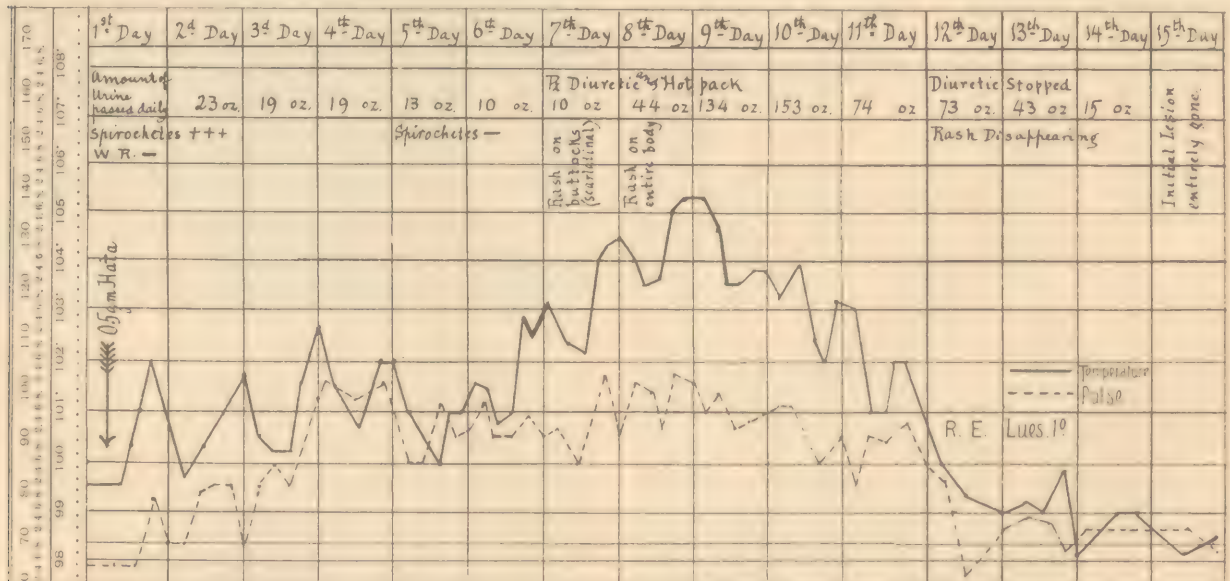


FIG. 14.—Illustrating Case XXVII. This chart shows an unusual rise of temperature to 105.4° F., eight days after the injection of 0.5 gramme of salvarsan. This was associated with urinary suppression; both responded to diuretics.

examination was refused. Period of observation, eight months.

CASE XXVII. Primary Syphilis: Unusual Reaction to the Treatment (This case has been reported in the *Interstate Medical Journal*, January, 1911). R. E., male, aged twenty-seven years. Referred by Dr. S. W. Bandler. Good general health. Initial lesion on shaft of penis, near corona, hard and typical in appearance, the size of a quarter. Duration two weeks. No secondaries. Inguinal glands indurated, not tender. Other glands negative.

November 4th: Examination for spirochætae, *positive*. Wassermann reaction, *negative*. Excision was suggested, but not permitted. To avoid any possible doubt as to the character of the lesion (in the absence of secondaries) patient was also examined by Dr. Ludwig Weiss, who confirmed the diagnosis. Examination of eyes, visceral organs, and urine, negative.

November 7, 1910, at a private sanatorium, 0.5 gramme hyperideal. Pain moderate, but in a few hours it extended down the thighs, and remained there for several days. Controlled somewhat by hot applications, and grain 14 morphine at bedtime. In the afternoon the temperature rose suddenly to 102° F. Pulse 76. A study of the temperature curve (Fig. 14) shows an unusually active response to the drug.

1st day,	99.5° to 102.0°	pulse	64 to 76.
2d day,	97.0° to 101.8°	pulse	68 to 80.
3d day,	100.1° to 102.6°	pulse	68 to 100.
4th day,	100.6° to 102.0°	pulse	98 to 100.
5th day,	102.0° to 101.0°	pulse	96 to 92.
6th day,	101.2° to 103.0°	pulse	92 to 96.
7th day,	103.0° to 104.5°	pulse	90 to 102.
8th day,	104.5° to 105.4°	pulse	90 to 102.
9th day,	105.4° to 103.8°	pulse	100 to 95.
10th day,	103.8° to 103.2°	pulse	95 to 90.
11th day,	103.2° to 100.8°	pulse	90 to 85.
12th day,	100.8° to 99.0°	pulse	85 to 72.
13th day,	99.0° to 98.2°	pulse	72 to 70.
14th day,	Normal.		Normal.

Interesting features of this case that are unusual were the very high temperature, partial suppression of urine, and coincident appearance of a generalized scarlatinal rash. The amount of urine passed on each day after the injection was as follows:

1st day,	amount not counted.
2d day,	23 ounces.
3d day,	19 ounces.
4th day,	19 ounces.
5th day,	13 ounces.
6th day,	10 ounces.
7th day,	10 ounces. Rash on buttocks (diuretic given).
8th day,	44 ounces. Rash on entire body, scarlatinal.
9th day,	134 ounces.
10th day,	153 ounces.
11th day,	74 ounces. Rash disappearing.
12th day,	73 ounces. Diuretic stopped.
13th day,	43 ounces.
14th day,	15 ounces.

The rash appeared coincidentally with the high temperature and urinary suppression; it first appeared on the buttocks (site of injection) and soon spread to the rest of the body (Fig. 15), including the face; the urinary condition was relieved by a strong diuretic and hot packs, with plenty of water internally. During all this time the patient did not feel unwell in the least, except for the pains in the legs, and in the arms. These were somewhat relieved by alcoholic rubs. There seemed to be a neuritis, possibly of arsenical character. The patient was rather dull and slept a good deal. Otherwise felt well. The tongue was coated with a yellowish white, thick, slimy fur. However, there can be no doubt that the entire complex of symptoms was due to faulty elimination of the drug, or supersensitiveness (idiosyncrasy) to the drug, or both.

November 11th. Spirochætae negative. Chancre soft and fast disappearing; glands negative. No infiltration or redness at the site of injection.

November 15th, discharged from hospital. Primary lesion gone, except a slight pinkish discoloration of the skin and slight thickening.

November 30th. Wassermann reaction + + +. Skin clear, glands negative, patient has gained about ten pounds. Eyes normal.

December 4th, Wassermann reaction + +; skin clear, patient normal and felt well.

July 25th, 1911, the patient reported feeling perfectly well; there have been no secondaries or other manifestations of the disease. He has gained much weight. Wassermann-Noguchi, slightly positive (+). August 7th, condition the same. Period of observation, nine months.

(b) CASES IN WHICH MARKED IMPROVEMENT FOLLOWED THE INJECTION WITHOUT RECURRENCE.

CASE XXVIII. Advanced Tabes Dorsalis: M. E., male, aged thirty years. Previous history as to primary and secondary syphilis, obscure. Present illness, duration one and one half years. Principal symptom, tabetic gait, which was very marked; also typical shooting pains in the legs. Walked with two canes; could not stand unaided. No involvement of the optic nerve. Wassermann reaction, strongly positive.



FIG. 15.—Illustrating Case XXVII. Photograph shows an unusual scarlatinal eruption covering entire body, on the seventh day after the injection of 0.5 gramme of salvarsan. This also disappeared on the administration of diuretics.

November 3, 1910, at the People's Hospital, received 0.5 gramme. No pain, at any time thereafter. Left the hospital twelve days later, apparently walking better. December 2, 1910, Wassermann reaction, +; gait much improved. February 27, 1911, walked unaided with one cane; looked and felt better; no pains; had gained in weight; tabetic gait not so marked. Wassermann and Noguchi, reactions, —. May 2, 1911, he reported feeling much better. Refused blood test. Period of observation, six months.

CASE XXIX. Tabes Dorsalis: C. G. M., male, aged thirty-six years. Referred by Dr. S. Ravich, of New Bedford, Mass. Primary syphilitic infection somewhat in doubt, but secondary lesions in the throat and about the anus appeared twelve years ago. Was treated on and off for three years, and had been well, except at intervals, when the sore throat reappeared; it was controlled by mixed treatment. First noticed pains and numbness in the legs about two years ago. Did not "feel sure" in his gait. Sight normal; about a year ago had incontinence of the bladder and rectum, but this was controlled

by the treatment. Romberg symptom, loss of patellar reflex, and Argyll Robertson pupil. Wassermann and Noguchi reaction, weakly positive.

November 22, 1910, at the People's Hospital, received 0.5 gramme. Slight pain. Left the hospital twelve days later, in good condition.

December 27th (one month after the injection) Dr. Ravich wrote: "Patient says he feels stronger and happier than before. Has gained ten pounds in weight. The shooting pains are not as marked as before, but still present. Vision unaltered. He always felt a little weakness in his legs, which is somewhat less marked than before. It is in the sensory symptoms that the patient feels the greatest improvement. He felt a sensation of numbness in the tips of his fingers and toes. This sensation has now diminished to a marked degree. The dormant sensation in the thighs has also improved greatly. He feels great improvement in the condition of the bladder. Micturition is of normal frequency (he used to suffer from too frequent micturition) and is accompanied by very little straining." Eyes normal, and Wassermann reaction weakly positive. (Massachusetts General Hospital).

March 25th (four months after the injection) patient reported his condition as being "the same as last report."

April 18, 1911, Dr. Ravich wrote: "His general condition is as good, if not better, than at the time of the last examination. The patient states he has completely regained the power of erection. Wassermann reaction, negative."

August 7, 1911, Dr. Ravich again kindly wrote: "The patient says he has better control of the flow of urine than before. Formerly there was a condition bordering on incontinence. He used to lose a drop or two involuntarily once in a while. All this is corrected now. On the other hand, he says that the act of micturition implies more straining now than before. . . His state of health in all other respects is the same as before." Period of observation, eight months.

CASE XXX. *Tertiary Syphilis Involving the Inguinal Glands*: C. A., male, aged forty-five years. Referred by Dr. L. T. Ashcraft, of Philadelphia, with the following history: There was no history of syphilis; five years ago, Dr. Ashcraft did a penile amputation and excised the chain of inguinal glands of the right side, the lesion being highly suggestive of carcinoma. This chain was very much broken down. Wassermann reaction, positive.

November 29, 1910, patient received 0.5 gramme. No pain. On that day the measurements of the thighs were as follows: Affected side, around the hip, 24.5 inches; around the ankle, 11.5 inches. On the normal side, hip, 20.5 inches, ankle, 9.5 inches.

December 7th, the patient appeared better. There was a slight decrease in the swelling of the affected side.

December 15th, Dr. Ashcraft wrote: "The thigh has decreased circumferentially. His condition is fairly good. The wound has not changed much. He seems to be developing pyelitis."

December 29, 1910, Wassermann reaction, negative.

January 3, 1911: "The wound shows decided evidences of improvement, but of course, as it was very deep, it is far from being healed. The thigh measurements have decreased from the original 24 inches in the thigh, and 18 in the calf, to 21 in the thigh and 13 3/4 in the calf."

May 3, 1911, the patient died of pneumonia. "He was, however, better from the injection." Period of observation, five months.

CASE XXXI. *Tertiary Syphilis with Perforation of the Hard Palate*: K. M., male, aged twenty-two years. Infected two years ago, and had received intermittent treatment. Presented a perforation of the hard palate, posteriorly, about half an inch in diameter. Speech markedly interfered with.

December 30, 1910, at the People's Hospital, he received 0.5 gramme. Moderate pain, which soon passed off. He left the hospital at the end of a week.

January 30, 1911, perforation is about the same, but speech was somewhat clearer, and patient had gained five pounds. Wassermann reaction, February 6, 1911, strongly positive. March 15th, Wassermann-Noguchi reactions, negative. Perforation had diminished in size perceptibly, and measured about one-eighth inch in diameter; speech much improved, and patient had gained eight pounds. July 30, 1911, his condition was the same as at last report. Period of observation, seven months.

CASE XXXII. *Syphilitic Periadentitis*: M. H., male, aged thirty years. Referred by Dr. H. P. Schlansky. History:—Primary infection three years ago, followed by usual secondaries. Received about thirty-five injections of mercury, and was apparently doing well, until two months ago, when the glands on the right side of the neck began to swell rapidly. The growth had continued in spite of mercury and iodides. A specimen of the tumor examined at Mount Sinai Hospital, proved the growth to be gummatous. November 3, 1910, Wassermann reaction, positive.

On November 13th, Wassermann-Noguchi reaction, strongly positive. On the 15th, at the People's Hospital, he was given 0.45 gramme, hyperideal. Owing to the presence of sugar and albumin in the urine, and a coexisting fatty heart, it was not deemed safe to give him a larger dose. He stood the injection usually well, having very slight pain, and moderate reaction. November 30th, Wassermann-Noguchi reaction, ++++. During the next two weeks, the growth diminished perceptibly in size, and became much softer, and the individual glands composing the mass could be made out. At that time, the mass began to cause pain for the first time, and his family refused permission for a second injection. He then went to Mount Sinai Hospital, where the mass was removed by Dr. A. A. Berg. After operation, the syphilitic induration extended to all the cellular planes of the neck. He returned to the hospital, where he was given mercury and iodides, and a second injection of salvarsan. The pathologist again reported the glands to be syphilitic in character. A great improvement in the induration was noticed thereafter, but one day, about two months after the operation (three months after the first injection of salvarsan), he sat up suddenly in bed, while still in the hospital, and fell back dead. No autopsy was granted. Cause of death was stated to be syphilitic myocarditis. Period of observation, three months.

In this case it will be observed that a distinct improvement followed the first injection, but unfortunately it did not last long. Possibly a larger dose, or a second injection soon after the first, might have saved him.

CASE XXXIII. *Cerebrospinal Syphilis*: L. S., male, aged thirty-two years. In the service of Dr. D. Robinson, at Beth Israel Hospital. History: Primary infection twelve years ago, and received some treatment; amount indefinite. Had been well since then, up to present illness. His wife had had three abortions and two healthy children. Four months ago, his wife noticed that he was becoming weaker physically, speech becoming jerky and incoherent, and a coarse tremor involving all the limbs. No pain anywhere. Ate and slept well, mentality clear. He kept on gradually growing weaker, his speech more indistinct, and was able to walk but a short distance without tiring. Perfect sphincter control; eyes normal. On admission, he gave these neurological signs: Spastic gait; Romberg; general spasticity; marked intention tremor; incoherent speech; Argyll Robertson pupil; dull mentality; eyegrounds normal (Dr. Born). Wassermann reaction, positive.

When I first saw him, on the invitation of Dr. Robinson, he was unable to talk, except to mutter unintelligently; he was confined to bed, but was not able to sit up, owing to the violent general muscular tremor. He walked into the operating room with the greatest difficulty. When told to hold out his hands, they swayed violently and were beyond control.

October 20, 1910, he received 0.45 gramme hyperideal. Practically no pain. October 24th, sat up in bed unassisted, and held out his hands for the first time with but a slight tremor. His speech seemed to be a little more distinct, and his mentality seemed less dull.

October 28th, tremor of hands and tongue less marked; much better.

November 10th, Wassermann reaction, slightly positive. November 18th, left the hospital, much improved.

May 2, 1911, Dr. Robinson reported that the patient's condition was about the same as when he left the hospital.

May 25, 1911, I saw the patient. He was by no means well, but his condition was far better than it was before the treatment. Refused a Wassermann test. Period of observation, seven months.

CASE XXXIV. Tertiary Ulcer of Leg Resistant to Mercury and Iodides: B. J., male, aged twenty-eight years. Primary infection seven years ago. Since then had had intermittent treatment. Six months ago, had ten injections of mercury; last treatment one month ago. Ulcer on right leg, duration seven months. It was almost half an inch in depth, and three quarters of an inch in diameter. Refused Wassermann test.

January 23, 1911, at the People's Hospital, received 0.6 gramme. No pain, but became dizzy and suffered slight shock. Felt well the next day. The ulcer gradually filled up, and on February 22, 1911 (one month after the injection) the entire cavity had disappeared, and its surface was flush with the adjoining skin. Strangely enough, epidermization did not take place for several months, in spite of additional stimulating treatment. June 6, 1911, however, the patient wrote that complete healing had taken place after taking mercury. Period of observation, four months.

CASE XXXV. Tertiary Syphilis with Perforation of Hard Palate: C. G. A., male, aged thirty-seven years. Primary lesion six years ago, followed by obstinate secondary lesions, which had left scars behind. Had been treated with pills all the time. Had a perforation of the hard palate as large as a twenty-five cent piece; also persistent ulcers on tonsils and pharyngeal wall. A faint pustular eruption on the back was also visible. Patient did not know how long the perforation has existed. Wassermann and Noguchi tests, +++.

November 23, 1910, at the People's Hospital, was given 0.5 gramme. Moderate pain, which persisted for some days. Patient left the hospital at the end of two weeks and was not heard from again until March 25, 1911, when his friend wrote saying, "Mr. A is feeling fine. To-night he told me that he has not felt so good for years." Period of observation, four months.

CASE XXXVI. Tertiary Syphilis with Considerable Destruction of Soft Palate: M. A., male, aged sixteen years. Referred by Dr. D. L. Morrison. History: Mother stated that the boy was born healthy, but began to show throat symptoms at the age of nine—seven years ago. Never had had any skin lesions. Mother and father both denied any history of syphilis; there were two other children in the family, both well. The boy had been taking "drops" for a long time, with little or no benefit. The entire uvula and both fauces had been destroyed. The boy's speech was hard to understand; he was undersized, and had just completed his school course. Wassermann reaction, ++++.

March 17, 1911, at the People's Hospital, received 0.5 gramme. No pain. Left the hospital a week later, much improved. April 7, 1911, Dr. Morrison wrote that "the improvement in this boy's case is decided and very apparent." Since then there had been a decided narrowing of the posterior arch left by the destruction of the soft tissues; the boy's speech improved markedly, and his general condition was also improved. He had been put on mixed treatment. May 5, general improvement maintained. Wassermann-Noguchi tests, mildly positive. July 20, 1911, condition same as before. Period of observation, four months.

CASE XXXVII. Cerebral Syphilis: S. D., girl, aged seven years. Referred by Dr. John H. Storer. History: Father had syphilis one year before marriage, was treated and considered himself cured. The patient, when five months old, fractured a femur, by rolling off a divan; this united in good condition. At the age of two years, a gumma on the under lip developed, as large as a walnut. This yielded to mercury and iodide of potassium. Soon thereafter, she began to have attacks, characterized by rigidity, almost loss of consciousness for a moment or two; these attacks usually came on on waking in the morning. These spells continued up to the present time, about once or twice a month, other times not quite so often. She had them as often as two or three times in one week. The four upper incisors of the second set of teeth had never appeared. She was somewhat peculiar, very bright, excitable, and it was very hard to make her obey. At times, she seemed to lack mental development, although she had a good memory for some things. At all times there was present a spirit of unrest and a lack of poise. The attacks seemed to be epileptiform in character, although not severe enough to be called epileptic. Their character was not very different or severer than they were

years ago. They did not respond in the least to bromides. Wassermann and Noguchi reactions, ++++.

It was decided to try the new remedy, and, December 14, 1910, at St. Mark's Hospital, she received 0.25 gramme intramuscularly. This was thought to be the largest dose for her age that would be safe. The child had practically no pain, and but a slight reaction. She could easily have taken the full dose, apparently. She left the hospital and was not seen again since. A letter received from the mother a month after the injection, stated that she noticed a marked improvement in the child's general condition, although she was by no means well. She had not had a "spell" for some weeks, and her general condition was highly encouraging.

May 4, 1911, (five months after the injection) the mother wrote: "She is still very nervous, but the 'spells' are less frequent and not as hard. One of her front teeth has grown in. She sleeps well, and looks well, but as for making her mind, it is almost impossible. In fact we see no change in her since last writing you."

August 7th, the mother wrote again: "She is improving very much, grows stronger and better every day."

In view of the distinct improvement in the child's condition soon after the treatment, some of which has still remained, a second treatment has been advised, but not yet acted upon. Wassermann reaction has been requested, but also refused. Period of observation, eight months.

CASES IN WHICH MARKED IMPROVEMENT WAS FOLLOWED BY CLINICAL RECURRENCE:

CASE XXXVIII. Primary and Secondary Syphilis: F. W. L., male, aged twenty-five years. Primary infection of three weeks' duration; secondaries just appearing. Typical Hunterian chancre on penis, adjacent to corona. Wassermann reaction, positive. November 15, 1910, at the People's Hospital, received 0.45 gramme, hyperideal. Moderate pain, lasting a day or two. Secondary roseola disappeared promptly, but chancre remained hardly affected, as it became softer and smaller very slowly. At the end of ten days, it was excised, and subjected to microscopic examination, with negative result. It did not appear different from the untreated chancre. All lesions then disappeared and the patient left town for a business trip.

February 7, 1911, (three months after injection), he reported clinically well; Wassermann-Noguchi reactions, negative. April 29th, negative. July 7, 1911, however (eight months after injection), he returned for observation, with a few small mucous patches on the lower lip, which had appeared a few days previously. Wassermann-Noguchi reactions, ++++. July 12th, he was given a second injection. He received 0.6 gramme, intravenously. The patches disappeared within forty-eight hours. This injection was followed by a third injection (also intravenous) on July 31st. On that date the Wassermann-Noguchi reactions were negative. He was last seen, August 12, 1911, feeling perfectly well. Period of observation, nine months. In this case it will be seen that the patient was clinically well for eight months after a single injection.

CASE XXXIX. Secondary Syphilis: S. J., male, aged twenty-three years. Patches in mouth and throat for past seven months, resistant to mercurial injections and internal treatment. Primary infection one year ago. Wassermann reaction, ++++.

October 24, 1910, at the People's Hospital, received 0.5 gramme, hyperideal. Moderate pain, lasting a few hours. Went home at the end of five days, without a trace of the patches, feeling perfectly well. The patient then disappeared from observation, but reappeared on May 10, 1911, (seven months after the injection), complaining of a soreness of the throat for the preceding few days. Examination showed the presence of two minute ulcerations on the tonsils; slight papular eruption on the left forearm. Wassermann and Noguchi reactions +. Refused a second injection.

Here we have another case of slight recurrence, seven months after the injection. July 25, 1911, under slight doses of mixed treatment, the ulcerations have passed away. Period of observation, nine months.

CASE XL. Tertiary Syphilis with Gummata: E. C. H., male, aged twenty-nine years. Primary lesion, nine years ago, on upper lip. Treated intermittently for one and one half year, with good result. Two weeks ago, noticed a thickening and redness of the tip of the nose, and simultaneously a purplish thickening and ulceration of the skin.

of one of the thighs. The latter broke down in several places. Wassermann and Noguchi reactions, strongly positive.

December 12, 1910, at the People's Hospital, received 0.6 gramme, hyperideal. No pain. Within a few days, the redness of the nose disappeared, and the gumma on the thigh showed marked evidence of improvement; and within a week it had entirely healed. The patient reported from time to time by telephone, that he was well. On February 7, 1911, he noticed a slight reddening of the nose, and went to a colleague, who found a slight positive Wassermann reaction. The nose improved rapidly under iodide and injections of gray oil. April 1, 1911, his physician reported him clinically well. Period of observation, four months.

CASE XLI. *Secondary Syphilis Resisting Mercury*: H. C. C., male, aged fifty-two years. Referred by Dr. Homer Gibney, with this history: Primary infection three months ago. Several weeks ago, ulceration of the throat developed, which persisted and grew more severe, in spite of continual internal treatment, with mercury administered by his physician. His pharynx and mouth were covered with large and small mucous patches. Voice was hoarse and husky. Wassermann reaction, ++.

March 21, 1911, at St. Mark's Hospital, received 0.6 gramme, intravenously. No reaction. Left the hospital following day, with every ulceration entirely gone. The recovery in this case was unusually quick and thorough. He remained perfectly well, until late in July, when the voice became hoarse again. Noguchi reaction, negative. July 31st, he received another injection, intravenously, and since then he had felt no return of the hoarseness. Period of observation, four months.

CASE XLII. *Tabes Dorsalis: Optic Atrophy: Gastric Crises: Marked Ataxia*: (Reported in the *Interstate Medical Journal*, January, 1911). J. M., male, aged thirty-six

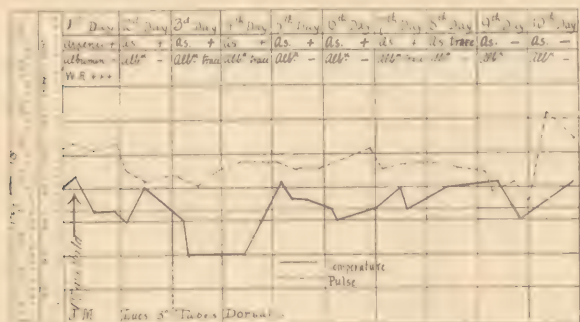


FIG. 16.—Illustrating Case XLII. This chart shows an unusual reaction, in that the temperature became subnormal on the third day after the injection of 0.5 gramme salvarsan.

years. Denied venereal history of any kind. First symptom of illness appeared six years ago, in the form of gastric pains, accompanied by occasional attacks of vomiting. Was treated for gastric disease until six months ago, when the diagnosis of tabes dorsalis was made by Dr. George J. Saylin, of Buffalo, N. Y. These symptoms were then present: Absence of knee jerk, marked ataxic gait, Romberg symptom, Argyll Robertson pupil, gastric crises with vomiting, shooting and lightning pains in legs. Optic atrophy, loss of flesh and strength. Wassermann reaction strongly positive. Urine negative as to sugar and albumin. Was put under treatment consisting of injections of salicylate of mercury and arsenic. Strychnine internally for the optic atrophy.

October 21, 1910, marked ataxia, necessitating use of two canes and other support. Stumbled in the dark. All diagnostic symptoms of tabes marked and unmistakable. Eyes examined by Dr. E. Gruening: "O. D. 3/100; O. S. 3/200. Both normal fields concentrically limited. Absolute color blindness. Optic atrophy."

Examination of viscera, heart, lungs, and kidneys, normal. Pulse 96, not very strong. Wassermann reaction, +++++.

At the earnest solicitation of the patient, and his assuming all liability as to the outcome, he was admitted to the People's Hospital.

October 24, 1910, 0.5 gramme. No pain whatever at the site of injection, during his entire stay in hospital. Six

hours after injection, pain appeared in the legs and around the chest. These did not differ in any way from his accustomed pains. Vomiting also set in on the second day, and continued for three days, after which period it ceased. Likewise the pains. The pain and vomiting did not differ in any way from his accustomed crises.

October 28th, out of bed, in ward. Walked without a cane. Thought his gait was less ataxic. With his eyes closed sways much less than previously. Pain absent. Eyesight not as good as before. Examination by Dr. Rosenbaum: "Atrophy somewhat advanced. Vision diminished. O. D. Fingers at five feet; O. S. Fingers at three feet. Previous to injection, O. D. Fingers at seven feet; O. S. Fingers at five feet." No infiltration or redness at the site of injection.

The temperature chart shows an unusual curve (Fig. 16). It will be seen that the patient reacted slightly on the day of the injection, by a lowering of the temperature to 98°, and on the third day there was a still further decline to 97° F. This decline was soon changed to a slight elevation, never exceeding 99.5°. It will be seen that the pulse did not share in the great lowering of the temperature. Arsenic was found in the urine eight days after the injection.

November 2, 1910, he left the hospital feeling very well, except for his sight. He walked easily without a cane, though he showed a distinct ataxic gait. Gain in weight, four pounds.

November 16th, came to office for observation. Walked without a cane. Felt much better.

December 3d. Communication from his physician, Dr. Saylin, stated: "Despite progressiveness of optic atrophy, gait and general condition show improvement. Patient is inherently hysteroneurasthenic,—yet, after careful observation, I can say that his condition has improved markedly, except his vision."

December 13th. Communication from Dr. Saylin, as follows: "Wassermann reaction, December 10th, taken by Dr. A. A. Thibaudau, is positive, but less strongly so than formerly. As regards the physical aspects of the case, I can but reiterate that there is a positive improvement. His gait is rather that of a blind man than that of a tabetic. Romberg's symptom, which was marked three months ago, is but slightly so now. He has gained in weight and complains less of weakness in his lower extremities and of the 'carpet' sensation. Vesical atony which was characteristic in his case, also shows improvement. However, he states positively that his sight became worse and became markedly so shortly after the administration of 606. Tests prove him right, and this raises a question as to future procedure."

It would appear from these data that with the exception of the effect on the optic atrophy, the treatment was highly beneficial. Unfortunately, a later report shattered whatever hope there was of a permanent improvement in this case. May 4, 1911, Dr. Saylin reported:

"I saw him at his home, day before yesterday. Briefly, I may state that he is as bad and his eyes surely worse than he ever was. He is totally blind. His gait is bad, his lightning pains are very severe. Vesical atony is again pronounced and sexual potency is impaired."

Here we have a case with distinct relief from the tabetic symptoms lasting several months, and a recurrence, with a loss of whatever improvement took place after the injection. It is also quite evident that the eyesight of the patient became much worse immediately after the administration of the salvarsan. Nevertheless in all fairness to the remedy may we not ask whether the blindness might not have come on even without the injection? How are we to know how much the injection had to do with the rapid progressiveness of the optic atrophy? Period of observation, six months.

CASE XLIII. *Paresis*: F. S. S., male, aged forty-eight years. Referred by Dr. Daniel T. Millsbaugh, of Paterson, N. J. This unusual case has been described in detail in the *New York Medical Journal*, July 1, 1911, to which the reader is referred for fuller particulars. Briefly, this was a typical case of paresis, with a distinct syphilitic history and a strong Wassermann reaction. October 27, 1910, he received 0.5 gramme, hyperideal. No pain.

The patient made remarkable progress soon after the injection, which lasted for several months. At that time, he was seized with a mild apoplectic stroke, which soon passed off, but brought with it a change in his condition.

which became worse from day to day. He finally died after another seizure, five months after the injection. Period of observation, five months.

CASE XLIV. *Syphilitic Gastritis*: D. S., male, aged

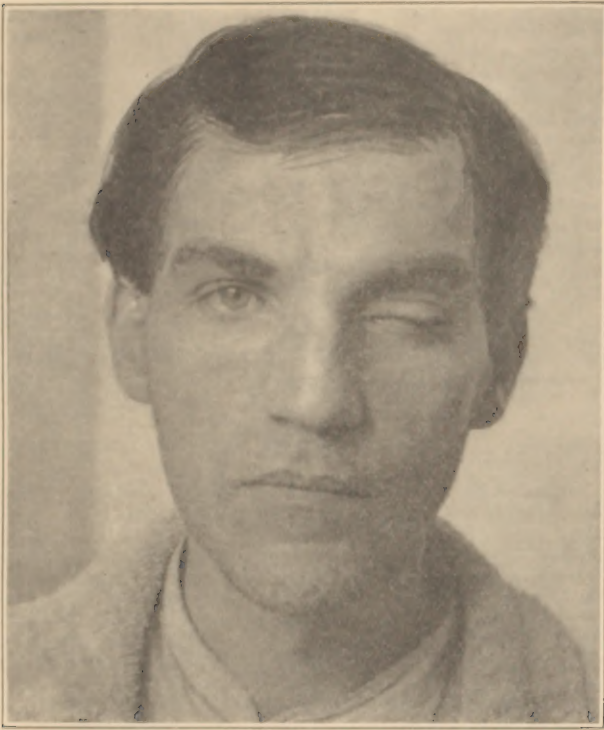


FIG. 17.—Illustrating Case XLVI. Complete ptosis of left eye for two years, resisting mercury and iodides.

forty years. Referred by Dr. L. Lesser. Primary infection eight years ago; at that time he received inunctions for several months. Then was well up to two years ago, when the present symptoms appeared. He had been taking large doses of iodides and had received about sixty or seventy mercurial injections. He complained of pain and tenderness over the stomach region and general malaise. He had been under the care of an eminent gastrologist, who diagnosed his case as syphilitic gastritis. There was a distinct leukoplakia of the tongue, slight adenopathy; pupils normal, slight Romberg symptom, and weak knee reflex. Wassermann reaction, ++++.

February 9, 1911, at the People's Hospital, he was given 0.6 gramme. Gastric contents examined immediately previous to the injection, made by Dr. A. Bassler, proved negative. May 5, 1911, patient reappeared for observation; he felt much better, though he complained of the return of his former pains to a lesser degree than formerly. Wassermann and Noguchi reaction, ++, July 2, 1911. Patient reported feeling the same as at last report. Period of observation, five months.

CASE XLV. *Secondary Syphilis: Iritis*: S. W., male, aged thirty-two years. Referred by Dr. J. B. Palmer. Primary infection, one year ago, followed ten weeks later by involvement of the throat. Seven months after infection, acute iritis set in, which resisted mercury and iodides for a long time. At present, iritis is under control. Wassermann reaction not determined, as he was still taking mercury and iodide.

February 9, 1911, at the People's Hospital, he received 0.5 gramme. Slight pain. Felt fine for one month, then began to see dark spots before the eyes, diagnosed by Dr. Palmer as neuritis. Mercury and iodides in increasing doses had been without any benefit. The throat had been perfectly well, and he had gained several pounds. Wassermann and Noguchi tests, negative. May 9th (three months after the injection), he wrote: "Excepting my eyes, I never felt better in my life, have a fine appetite and have gained six pounds." July 15, 1911, he reported the same condition. Period of observation, five months.

CASE XLVI. *Tabes Dorsalis with Ptosis of Eyelid*: C. P., male, aged twenty-eight years. Primary infection eight years ago. Treated eight months, and felt well until July, 1909. Present trouble began at that time, with abdominal pains and gastric crises, followed by shooting pains and numbness in feet and legs; this was soon followed by paralysis of the left eyelid and partial optic atrophy, with eversion of the corresponding eye (Fig. 17). Since then he had been treated continually with mercury and iodides in large doses, up to the point of toleration. Did not respond well to the treatment. August, 1910, at the City Hospital, was treated with mercurial injections for five weeks, without benefit.

When I first saw him (October, 1910), he was in very poor shape, having diminished in weight from 165 to 103 pounds in the last six months. Pains were very severe and almost constant, requiring morphine several times daily. Bladder and rectum not under control at times; straining at urination constant. Romberg, Argyll Robertson pupil, and loss of knee jerk present. Wassermann reaction, negative.

October 24, 1910, at St. Mark's Hospital, he received 0.45 gramme, intramuscularly. No pain. Two days later, the ptosis of the left eye had entirely disappeared, and he was able to move his eyelid and the eye, in any direction at will (Fig. 18). He had no pain in the abdomen for the first time in a long while. The sight in the left eye was much improved, and he was easily able to count the fingers at a distance of fifteen feet; this he was unable to do previously. A neurological examination made by Dr. M. Neustaetter, October 29th (five days after the injection), was as follows: "Very slight ptosis in the left eye. Paralysis of the inferior and internal recti of this eye. Marked analgesia, no anesthesia, deep muscular sense intact on left side of body, but affected in right lower extremity. Ataxia in lower extremities and right upper extremity. Marked hypotonia in lower extremities. Diagnosis: Tabes, with gummatous infiltration of the abducens and oculomotor."

Three weeks after the injection, however, a gastric crisis set in, with severe pain and the usual vomiting. Morphine

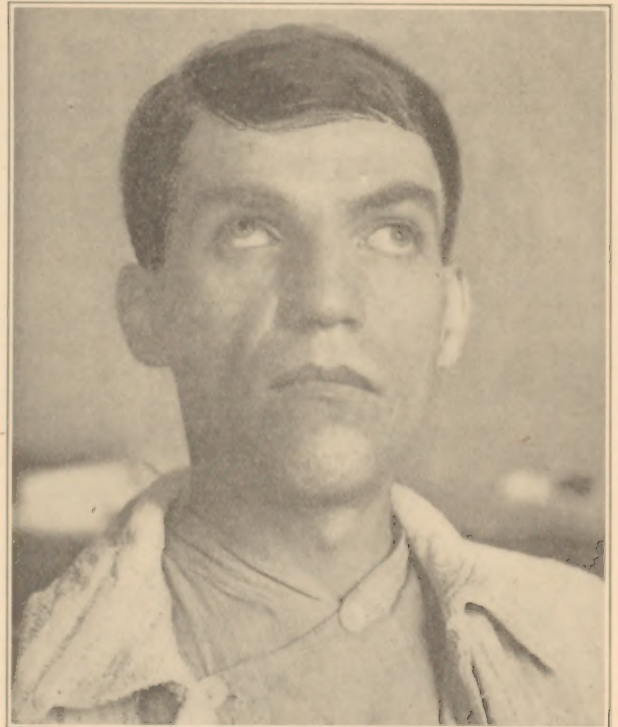


FIG. 18.—Illustrating Case XLVI. Ptosis of left eye relieved completely within five days after the injection of 0.45 gramme salvarsan. The relief has persisted up to date. (See also Fig. 17.)

in ordinary doses was unable to control the pain. Until then morphine was not required. This continued up to November 21st, when it was deemed necessary and wise to

give him a second injection. On that date he received 0.5 gramme. Contrary to the result in the first injection, he at once felt a severe pain in the right leg and thigh, which was of the nature of an acute neuritis. This pain continued for a long time. His general condition gradually returned to its former state, and he lost the fourteen pounds that he had gained. His eyelid, however, retained its improvement. Sight in the affected eye, fairly good, fingers being discerned at twenty-five feet.

January 7, 1911, Dr. Neustaedter made a second examination and found: "Ptosis markedly improved; motor oculi still paralyzed, optic atrophy in left eye marked. Gait markedly worse, patient being extremely atactic in lower extremities, upper extremities being free from ataxia. Deep muscular sense in toes of right foot entirely gone; complete anaesthesia and analgesia in peroneal and tibial group of muscles of right extremity. Absence of faradaic response in these muscles and reaction of degeneration present; also qualitative diminution in response to galvanic current. This would show that we have here a nerve degeneration. The trophic disturbances, such as bed sores and diminution in size of the right limb muscles and their flabbiness, and partial atrophy, would substantiate this."

Reports from the patient, dated February 19th, April 10th, and July 15th, stated that his condition was about the same as, if not somewhat worse, than when this last report was made. Morphine was resorted to for the pain, and the gastric crises came on with their previous frequency and severity.

Here we have a case which responded beautifully for nearly a month, followed by recurrence. There has been an improvement, however, in the paralysis of the eyelid, due to the clearing up of a gummatous process. This improvement has lasted nine months, and appears to be permanent. To offset this improvement, however, the second injection, which it was hoped would increase the improvement which followed the first, actually brought on a nerve degeneration of the right lower extremity. Whether this degeneration is due to a chemical or mechanical cause, cannot be determined. The Wassermann reaction in this case was uniformly negative, in three examinations at various times, before and after treatment. Period of observation, nine months.

CASE XLVII. *Tertiary Syphilis*: M. M., female, aged forty years. History: Primary infection uncertain as to date, but secondaries began to appear about three years ago. At that time her husband was being treated for syphilis, and she assumes that she was infected through him. She has received treatment intermittently, but nevertheless the nasal bones became involved and have undergone almost complete destruction. For the past year and a half there had been a most obnoxious ozæna, which has not yielded to mercury or iodides. Wassermann reaction, ++++.

December 30, 1910, at the People's Hospital, she received 0.5 gramme. Slight pain, which persisted for about ten days. Within a week the ozæna had improved very greatly, so that there was barely any odor perceptible. Unfortunately this improvement was but shortlived, and the ozæna soon returned. May 7, 1911, the ozæna has returned, but her general health has improved considerably. On June 25, 1911, the same report was made. Period of observation, six months.

(d) CASES IN WHICH NO CHANGE FOLLOWED THE INJECTION.

CASE XLVIII. *Total Optic Atrophy*: G. H., male, aged twenty-six years. Totally blind. Duration one and one half year. Primary infection, 1903, followed by treatment for seven months. Had been well since then, as far as syphilitic lesions were concerned. On January 14, 1908, the right eye became blind during the night. There had been no premonitory symptoms of any kind, and the blindness was complete. The condition was diagnosticated as optic atrophy due to syphilis, but it made no response whatever to mercury and large doses of iodides. Seven or eight months later the left eye became involved in the atrophic process, and within two weeks total blindness set in. Examination of the eyes, November 15, 1910, showed total optic atrophy in both eyes; no perception of light. Wassermann reaction, ++.

November 15, 1910, at the People's Hospital, received

0.6 gramme. Moderate pain, which became worse and lasted several days. On the day after the injection the patient insisted that he saw flashes of light before his eyes. He declared that he had never seen them before. They were so strong and constant that they interfered with his sleep. Under moderate doses of veronal, given at bedtime, they disappeared and he was enabled to sleep. He had no pain in the eyes at any time.

December 5, 1910. Patient stated he felt good generally; had gained seven or eight pounds; still saw the flashes, and was unable to sleep on that account. Sight not affected. The flashes stopped soon after this date.

December 19, 1910, received another injection, 0.5 gramme. Slight pain, lasting one hour. After this injection he saw no flashes, and had not seen any since. Wassermann and Noguchi reactions (three days after the second injection), ++++. February 7, 1911, Wassermann and Noguchi tests, negative; May 4, 1911, Wassermann positive, Noguchi, doubtful.

It will be observed that in this case of double complete optic atrophy of syphilitic origin, the remedy was of no avail, as was to be expected, though the patient gained about eight pounds. The only effect of the treatment was to produce flashes before the eyes, which lasted about a month. The Wassermann reaction was also changed from positive to negative or doubtful. Period of observation, six months.

CASE XLIX. *Cerebrospinal Syphilis: Hereditary Syphilis: Third Generation*: M. E., male, aged fifteen years. History: The ancestry of this patient was of unusual interest. Both parents were of unusual intelligence and culture. The father was perfectly well, as far as he could recall, until the time of his marriage, when a cutaneous lesion about the genitals developed which seemed to baffle the best dermatologists and syphilographers in this country and Europe. Shortly after their marriage a lesion of a somewhat similar character developed in the wife, also about the genitals. This lesion has also never been positively diagnosticated. Since then unmistakable evidences of syphilis have developed in both parents, which have responded to mercury and iodides. This child was born within a year or two after the marriage, and when a few weeks old, typical symptoms of syphilis developed. This diagnosis was made by an eminent dermatologist in this city, who declared at the time that the child would outgrow the disease. He advised against the use of mercury. The parents were both positive as to these features of the history.

The cutaneous lesions passed away under treatment, and for several years the child seemed bright and normal in every way. But, at about five years of age, epileptiform convulsions appeared which increased in frequency and severity. During the past four years the boy had had as many as twenty-five convulsions in a single day, all of great severity. He fell frequently, and suffered more or less severe injuries. For several years past he had been deprived of all intelligence, and had been reduced to the condition of an imbecile. He could not stand or walk without assistance.

In the hope that something might be done, it was decided to give him an injection of salvarsan. The Wassermann reaction was strongly positive. A neurological examination made immediately before the injection by Dr. M. Neustaedter was as follows: "There is present a complete right hemiplegia of a spastic character, with exaggeration of reflexes; clonus and Babinski sign. The complete motor and sensory aphasia point, to an involvement of the left hemisphere and a descending degeneration of the lateral tracts of the spinal cord. On the left side, the patellar reflex is exaggerated, supertonus in extensor muscles of the leg, and paresis. The expression is stupid, intelligence dull. Trophic disturbances: Integument of the nose, swollen and with a reddish discoloration; lips and cheeks puffed. Sphincters ani and vesicæ disturbed.—involuntary defæcation and micturition. Diagnosis: Cerebrospinal syphilis, with secondary degeneration in the motor cortical region and lateral tracts, and destruction of the Island of Reil."

January 27, 1911, at St. Mark's Hospital, he received 0.5 gramme. He had slight pain, which increased perceptibly and lasted for several months. This was seen by the fact that he cried out in pain whenever his leg or thigh on the injected side was moved or handled. Half an hour after

the injection, however, he was able to sit on a chair, while his bed was being cleaned.

It appeared to those who were observing the patient, including his mother, that he showed unmistakable evidences of improvement in mentality for three or four days after the injection. His face took on a more natural color and look, the puffiness disappeared, and he seemed to take more interest in his surroundings. But he soon returned to his former state, and remained so.

It is interesting to note in this connection that his father reported (July 26, 1911) that the boy was in very bad condition to a few weeks ago, when a period of remission seemed to have set in, and he had shown evidences of improved mentality, as for instance, in being able to play with his toys, and say a few words, "mamma" and "papa." He recognized his parents.

Of still further interest, is the fact that both father and mother have been under antisyphilitic treatment since this child was born; that three healthy and normal children were born after this child; and that the father had but recently discovered the fact that his father (the boy's grandfather) had suffered for many years with syphilis. When he has apparently the rare condition of syphilis occurring in three successive generations. Period of observation, six months.

CASE I. *Tabes Dorsalis: Osteomyelitis of Lower Jaw:* F. L., male, aged forty years. Married, and the father of a healthy child two and one half years old. Referred by Dr. Charles Pollock, of Brooklyn. Primary infection, eleven years ago; was treated for two years internally. Has had no symptoms of syphilis since, except a chronic abscess of the left lower jaw, which had resisted surgical and antisyphilitic treatment. Present complaint (November, 1910), pains in the spine and chest (girdle sensation), coming on at intervals, for the past five years. During these attacks he was incapacitated from his work. Examination: Romberg, Argyll Robertson pupil, present, loss of knee reflex. Examination of the eyes by Dr. Vincent Barber, negative as to optic nerve lesions. A radiographic plate of the left hand (taken by Dr. Harry Isaacs) showed "on the first metacarpal and the second and third proximal phalanges, a subperiosteal deposition of bone, suggesting a syphilitic lesion."

November 18, 1910, he received 0.6 gramme hyperideal, at the People's Hospital. He had moderate pain, lasting several days. He left the hospital at the end of a week feeling somewhat better as far as his pains were concerned, and the discharge from the sinus in the jaw seemed to be less than formerly. He then disappeared from view, but returned for observation, June 27, 1911. On examination it was found that his tabes had remained stationary, uninfluenced by the treatment, but the wound in the jaw had improved somewhat. It was quite likely that a second injection might have been of great advantage. This he refused. Period of observation, seven months.

In addition to these fifty cases there are three cases of interest which, for obvious reasons, have not been included in this report.

CASE I. *Suspected Primary Chancre of the Cervix:* Mrs. B. C., aged twenty-five years. Referred by courtesy of Dr. Dougal Bissell, at his service at the Woman's Hospital. History: Married four years, one child aged twenty-two months; supposed miscarriage, July, 1910, of one month. On examination, August, 1910, this condition was present: A complete procidentia, erosion of entire cervix, cervix very hard. After six weeks in bed and tamponing, a healthy mucous surface covered the cervix. At that time she complained of leucorrhœa, backache, bearing down and dragging pain on left side, and rheumatic (?) pains in head, especially severe at night; enlargement of cervical glands, on both sides. Wassermann reaction (Dr. Kaplan), positive. Husband admitted having contracted syphilis four months before the patient presented herself for treatment.

October 10, 1910, at the Woman's Hospital, she received 0.6 gramme. For several weeks she complained of pain and stiffness in the buttock, but this soon passed off. She left the hospital October 28th; the cervix had resumed its normal softness, and she felt quite well. She has since appeared from view.

CASE II. *Tabes Dorsalis: Death Twelve Days After the Injection:* A. B., male, aged thirty-eight years; patient of

Dr. D. S. Millsbaugh, of Paterson, N. J. This case has already been fully reported in the *New York Medical Journal*, July 1, 1911. Briefly, the man was injected, October 28, 1910, and on the following day he went into a stuporous condition, suggestive of uræmia, from which he did not emerge. He died twelve days later, with symptoms that pointed to uræmia as the cause of death. Autopsy was refused.

CASE III. *Inherited Syphilis:* M. T., infant, two months old. Referred by courtesy of Dr. Charles G. Kerley, at the New York Nursery and Child's Hospital. History: Nothing known of family history; mother seemed to be in fair condition. When born the infant weighed seven pounds, three ounces, temperature 99° F., condition poor. Ophthalmia neonatorum; organs normal, but abdomen distended; papular eruption on whole body; skin dry; hands and feet exfoliated. Under bichloride of mercury, internally, the child did rather poorly. October 31, 1910, on the invitation of Dr. Kerley, I gave the patient an intramuscular injection of 0.033 gramme. The dose was a rather small one, but it was the dose that I had seen Wechselsmann use in his pioneer work in Berlin and which gave splendid results. The infant stood the treatment well and within a few days most of the papules on the face and body had faded perceptibly. There was a slight temperature reaction, which lasted but a few days, but the infant showed no ill effect from the treatment. There was a slight gain in weight which lasted for some time, but soon receded. November 24, 1910, I repeated the injection, with a dose much larger than the first, namely, 0.15 gramme. Apparently, there was some slight benefit, but the child was soon put on mercury again. December 8, 1910, the child died. Cause of death not given.

CONCLUSIONS.

As a result of a study of these data we may conclude:

1. Of fifty cases, studied clinically for periods varying from three to ten months (an average of 6.4 months), after a single injection, twenty-seven (54 per cent.) may be considered clinically "cured"; ten (twenty per cent.) improved materially, and have not yet suffered recurrence; ten (twenty per cent.) improved, but developed clinical recurrence later; three (six per cent.) showed no change as a result of the treatment.

2. When clinical recurrence took place it occurred most frequently in the first three months after treatment. Evidently one injection was not sufficient to produce the desired result. One case recurred after seven months, and one after eight months. Repetitions of the treatment should be given within one month, to insure the best results.

3. The Wassermann reaction remained positive in thirty-three per cent. of the cases, and became negative and remained so in thirty per cent. of the cases for periods averaging four to five months.

4. In the cases considered "cured," the reaction became negative in forty-one per cent., and remained positive in thirty per cent.; in the cases which improved without recurrence, forty per cent. became negative and twenty per cent. remained positive; of the cases improved, with recurrence, thirty per cent. became negative and fifty per cent. remained positive. This showed that the Wassermann reaction is more likely to change from positive to negative in cases which also respond clinically to the influence of the remedy than in cases which do not show this favorable result.

5. The positive reaction is apt to remain uninfluenced in cases in which clinical recurrence takes place.

6. In the primary cases the reaction became negative in thirty-three per cent., and remained posi-

tive in fifty per cent. of the cases; in the secondary cases the reaction became negative in fifty per cent., and remained positive in thirty-six per cent. of the cases; in the tertiary cases the reaction became negative in fifteen per cent. and remained positive in twenty-two; in the parasyphilitic cases the reaction became negative in fifty per cent. and remained positive in forty per cent. of the cases.

7. The therapeutic effect of a single injection of salvarsan is equivalent in potency to a course of mercury and iodides, in a large proportion of cases. This is particularly true in primary cases and in cases which have not responded previously to vigorous treatment with mercury and iodides. We have in this new remedy the most powerful and trustworthy medium for the conquest of syphilis that has ever been known. It will not entirely supplant mercury and iodides, but it will undoubtedly take its place as the foremost remedy at our command. We are still in ignorance of the best method

of using salvarsan; we do not know the maximum curative dose, nor do we yet know the best method, nor how often it should be repeated. All of this information will come to us within a reasonable time, and we shall then be better able to judge of its permanent value. Of one thing we are certain, namely, that salvarsan has come to stay, and that it will certainly play the principal role in the conquest of syphilis.

I desire here to tender my thanks to Gehrmrat Professor Ehrlich for the generous supply of the remedy which he placed in my hands last October which made possible the treatment of the cases herein reported; also to the members of the staff of the People's and St. Mark's Hospitals, for their courteous cooperation in the observation and treatment of these cases, and to Dr. M. Neustaedter and Dr. M. Rosenbaum, for their neurological and ophthalmoscopic examinations, respectively.

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